(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 291 969 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication of patent specification: **16.02.94**

(51) Int. Cl.[5]: **C07D 257/04**, C07D 403/10, C07F 7/22

(21) Application number: **88108005.5**

(22) Date of filing: **19.05.88**

(54) **Tetrazole intermediates to antihypertensive compounds.**

(30) Priority: **22.05.87 US 53198**

(43) Date of publication of application: **23.11.88 Bulletin 88/47**

(45) Publication of the grant of the patent: **16.02.94 Bulletin 94/07**

(84) Designated Contracting States: **AT BE CH DE ES FR GB GR IT LI LU NL SE**

(56) References cited:
EP-A- 0 028 834
EP-A- 0 106 140
EP-A- 0 253 310

JOURNAL OF ORGANOMETALLIC CHEMISTRY, vol. 33, 1971; K. SISIDO et al., pp. 337-346&NUM;

ADVANCED ORGANIC CHEMISTRY, by J. March, John Wiley & Sons, 1985; p. 597&NUM;

(73) Proprietor: **E.I. DU PONT DE NEMOURS AND COMPANY**
1007 Market Street
Wilmington Delaware 19898(US)

(72) Inventor: **Aldrich, Paul Edward**
306 Spalding Road
Wilmington, DE 19803(US)
Inventor: **Pierce, Michael Ernest**
7 Dale Court
Wilmington, DE 19810(US)
Inventor: **Duncia, John Jonas Vytautas**
35-B Martine Court
Newark, DE 19711(US)

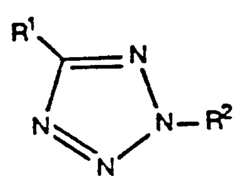
(74) Representative: **von Kreisler, Alek, Dipl.-Chem. et al**
Patentanwälte
von Kreisler-Selting-Werner
Postfach 10 22 41
D-50462 Köln (DE)

EP 0 291 969 B1

Description

This invention relates to substituted tetrazoles useful as intermediates in the preparation of antihypertensive compounds.

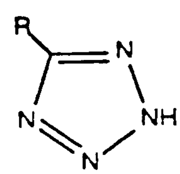
S. Kozima et al., J. Organometallic Chem., 33, 337, (1971) and ibid, 92, 303 (1975) describes substituted tetrazoles of the formula:



wherein

R^1 is lower alkyl, benzyl, lower alkenyl or phenyl optionally substituted by nitro, lower alkyl, lower alkoxy or halogen; and R^2 is SnR_3.

R. Lofquist et al., J. Amer. Chem. Soc., 80, 3909 (1958) describes substituted tetrazoles of the Formula:



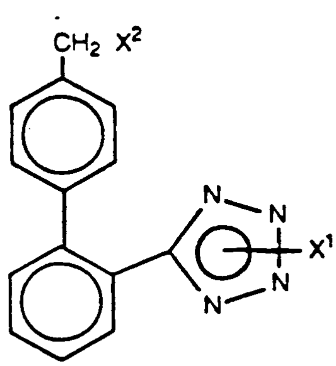
wherein

R is lower alkyl, benzyl, cycloalkyl of 4 carbon atoms, n-heptyl perfluoro, $-SR^1$ where R^1 is lower alkyl, benzyl; $-(CH_2)_nR^2$ where R^2 is OH, CO_2R^1, OR^1, SO_3Na and n is 1 or 2; or phenyl optionally substituted with amino, lower alkoxy, lower alkyl, nitro or cyano.

W. Beck, et al., Chem. Ber., 116, 2691 (1983) describes the preparation of 2-trityl-5-phenyl tetrazole.

EP-A-0 106 140 discloses tetrazol-substituted biphenyl compounds which are reported to be useful in the reduction or control of blood lipids in animals.

According to the present invention, there are provided novel compounds of Formula (I) which are tetrazole intermediates useful for the preparation of antihypertensive compounds. These tetrazoles have the Formula:

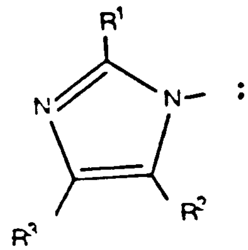


(I)

wherein

X^1 is H $Sn(R)_3$, $-C(Phenyl)_3$, p-nitrobenzyl, or β-propionitrile;

X^2 is Cl, Br, I, O-tosyl, OH, O-mesyl, or



R	is alkyl of 1-6 carbon atoms, phenyl or cyclohexyl;
R^1	is alkyl of 3-10 carbon atoms, alkenyl of 3 to 10 carbon atoms, alkynyl of 3 to 10 carbon atoms, and benzyl substituted with up to two groups selected from alkoxy of 1 to 4 carbon atoms, halogen, alkyl of 1 to 4 carbon atoms, nitro and amino;
R^2	is phenylalkenyl wherein the aliphatic portion is 2 to 4 carbon atoms, $-(CH_2)_m$-imidazoyl-1-yl, $-(CH_2)_m$-1,2,3-triazolyl optionally substituted with one or two groups selected from CO_2CH_3 and alkyl of 1 to 4 carbon atoms, $(CH_2)_m$-tetrazolyl, $-(CH_2)_nOR^4$;

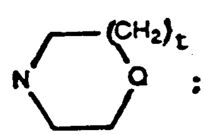
$$-(CH_2)_nO\overset{O}{\overset{\|}{C}}R^5;\quad -CH{=}CH(CH_2)_s\overset{O}{\overset{\|}{C}}R^6;$$

$$-CH{=}CH(CH_2)_s\underset{R^5}{\underset{|}{C}}HOR^7;\quad -(CH_2)_n\overset{O}{\overset{\|}{C}}R^6;\quad -(CH_2)_nNH\overset{O}{\overset{\|}{C}}-OR^8;$$

$-(CH_2)_nNHSO_2R^8$; $-(CH_2)_mF$;

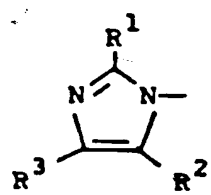
$$-\overset{O}{\overset{\|}{C}}R^6;$$

R^3	is H, F, Cl, Br, I, NO_2, CF_3, or CN;
R^4	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl or benzyl;
R^5	is H, alkyl or perfluoralkyl of 1 to 8 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl or benzyl;
R^6	is H, alkyl of 1-5 carbon atoms, OR^9 or $NR^{10}R^{11}$;
R^7	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl, benzyl, acyl of 1 to 4 carbon atoms, phenacyl;
R^8	is alkyl of 1 to 6 carbon atoms or perfluoroalkyl of 1 to 6 carbon atoms, 1-adamantyl, 1-naphthyl, 1-(1-naphthyl)ethyl, or $(CH_2)_pC_6H_5$;
R^9	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, or phenyl;
R^{10} and R^{11}	independently are H, alkyl of 1 to 4 carbon atoms, phenyl, benzyl or taken together to form a ring of the Formula



Q	is NR^{12}, O, or CH_2;
R^{12}	is H, alkyl of 1 to 4 carbon atoms, or phenyl;
m	is 1 to 5;
n	is 1 to 10;
s	is 0 to 5;
p	is 0 to 3;
t	is 0 or 1.

with the proviso that when X^1 = H then X^2 cannot be



Preferred compounds are those of Formula (I) where:

X^1 is H, $Sn(R)_3$ or -C(phenyl)$_3$ where R is alkyl of 1 to 6 carbon atoms or phenyl; or

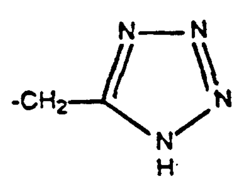
X^2 is Br, Cl, or the substituted imidazole; or

R^1 is alkyl, alkenyl or alkynyl of 3 to 7 carbon atoms; R^2 is $-(CH_2)_mOR^4$;

$$-(CH_2)_m O\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH-\underset{}{\overset{R^5}{\overset{|}{C}}}HOR^7$$

$$-(CH_2)_m\overset{O}{\overset{\|}{C}}-R^6; \quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8;$$

$-(CH_2)_mNHSO_2R^8$;



; or $-\overset{O}{\overset{\|}{C}}R^6$;

R^3 is H, Cl, Br, or I;

R^4 is H, or alkyl of 1 to 4 carbon atoms;

R^5 is H, or alkyl of 1 to 4 carbon atoms;

R^6 is H, alkyl of 1 to 5 carbon atoms; OR^9; or N O;

R^7 is H, alkyl of 1 to 4 carbon atoms, or acyl of 1 to 4 carbon atoms;

R^8 is CF_3, alkyl of 1 to 6 carbon atoms or phenyl;

m is 1 to 5.

Specifically preferred compounds are those of Formula (I) where:

(1)

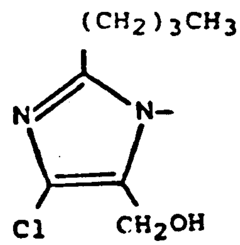
X^1 is $Sn(CH_3)_3$, $Sn(Ph)_3$, Sn(n-Bu)$_3$, C(Phenyl)$_3$, or H; and

X^2 is Br.

(2)

X^1 is $Sn(CH_3)_3$ or C(Phenyl)$_3$: and

X^2 is

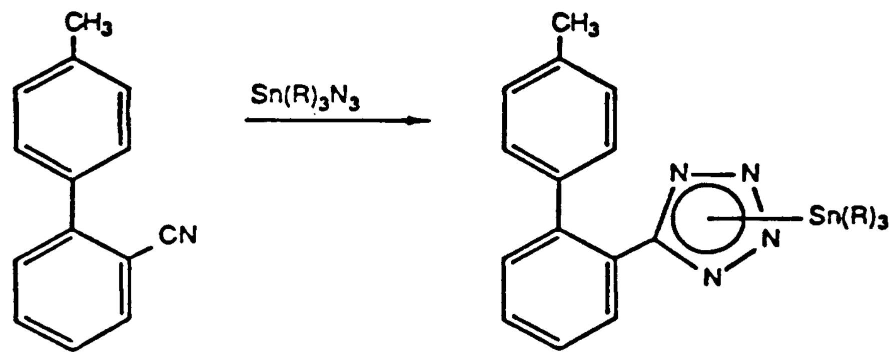


Synthesis

The novel compounds of Formula (I) may be prepared using the reactions and techniques described in this section. The reactions are performed in a solvent appropriate to the reagents and materials employed and suitable for the transformation being effected. It is understood by those skilled in the art of organic synthesis that the functionality present on the imidazole and other portions of the molecule must be consistent with the chemical transformations proposed. This will frequently necessitate judgment as to the order of synthetic steps, protecting groups required, deprotection conditions, and activation of a benzylic position to enable attachment to nitrogen on the imidazole nucleus. Throughout the following section, not all compounds of Formula (I) falling into a given class may necessarily be prepared by all methods described for that class. Substituents on the starting materials may be incompatible with some of the reaction conditions required in some of the methods described. Such restrictions to the substituents which are compatible with the reaction conditions will be readily apparent to one skilled in the art and alternative methods must then be used.

Compounds of the Formula (I), where X^1 is $Sn(R)_3$ and R is alkyl of 1 to 6 carbon atoms or phenyl and X^2 is imidazoyl where R^1 is n-butyl, R^3 is Cl, and R^2 is hydroxymethyl may be prepared by the 1,3-dipolar cycloaddition of trialkyltin or triphenyltin azides to the appropriately substituted nitrile (II) (Scheme I). An example of this technique is described by S. Kozima, et al., J. Organometallic Chemistry, 33, 337 (1971). Other required nitriles and trialkyl or triaryl tin azides are either available commercially, or may be prepared using techniques and methods reported in the chemical literature, J. Luijten et al., Rec. Trav. Chem., 81, 202 (1962).

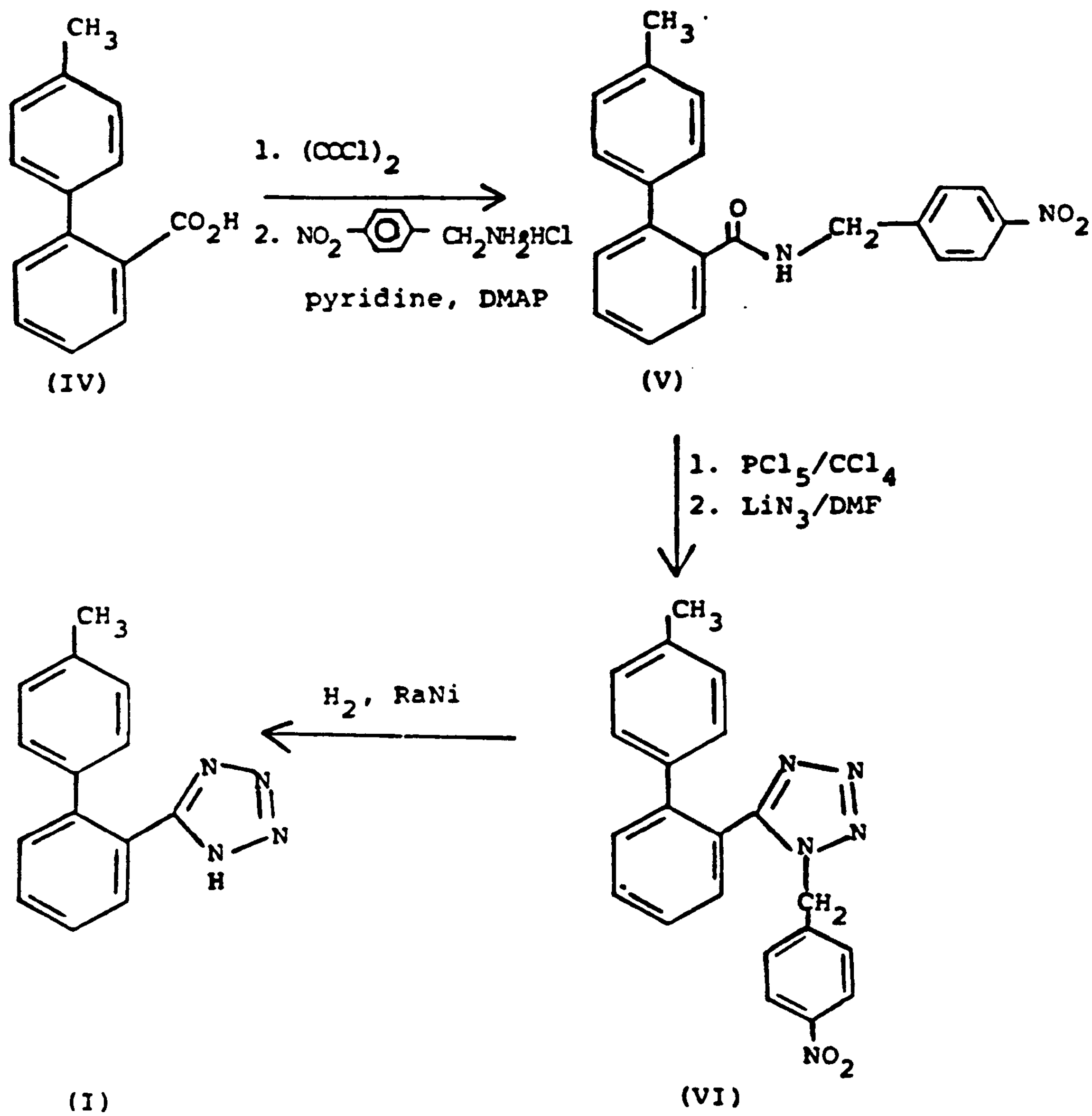
Scheme I



(II) (III)

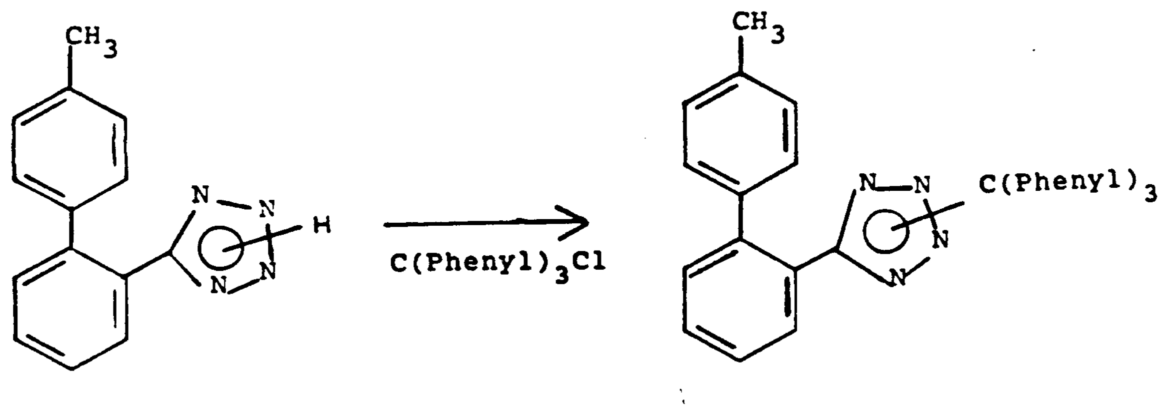
Compounds of the Formula (I), where X^1 and X^2 are H, which compounds as such are, however, not according to the invention, may be prepared by removal of a suitable protecting group on the tetrazole nucleus. Suitable protecting groups for the tetrazole moiety include p-nitrobenzyl, β-propionitrile, triphenylmethyl, and trialkyltin which are prepared via the following methods. The nitrobenzyl protecting group is attached as shown in Scheme II. The acid (IV) is converted to the intermediate acid chloride with oxalyl chloride under standard conditions. The acid chloride is converted to the amide (V) by condensation with 4-nitrobenzylamine hydrochloride in pyridine in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP). The amide (V) is converted to the intermediate iminoylchloride via reaction with phosphorus pentachloride in carbon tetrachloride. One example of this method is described by H. Ulrich, The Chemistry of Imidoyl Halides, Plenum Press, N.Y., N.Y. (1968). The intermediate iminoyl chloride is converted to the tetrazole (VI) with lithium azide in dimethylformamide (DMF). An example of this method is described by Elderfield, Heterocyclic Compounds, John Wiley and Sons, (1967). The protected tetrazole (VI) is then hydrogenated at 344.7 kPa (50 psi) in the presence of a catalytic amount of W6 Raney nickel in ethanol to yield (I). The required acid (IV) is available commercially or may be prepared using techniques and methods reported in the chemical literature.

Scheme II



The triphenylmethyl group is attached as shown in Scheme III. The tetrazole (I) reacts with triphenylmethylchloride in methylene chloride containing triethylamine as the base under standard conditions to yield the protected tetrazole (VII).

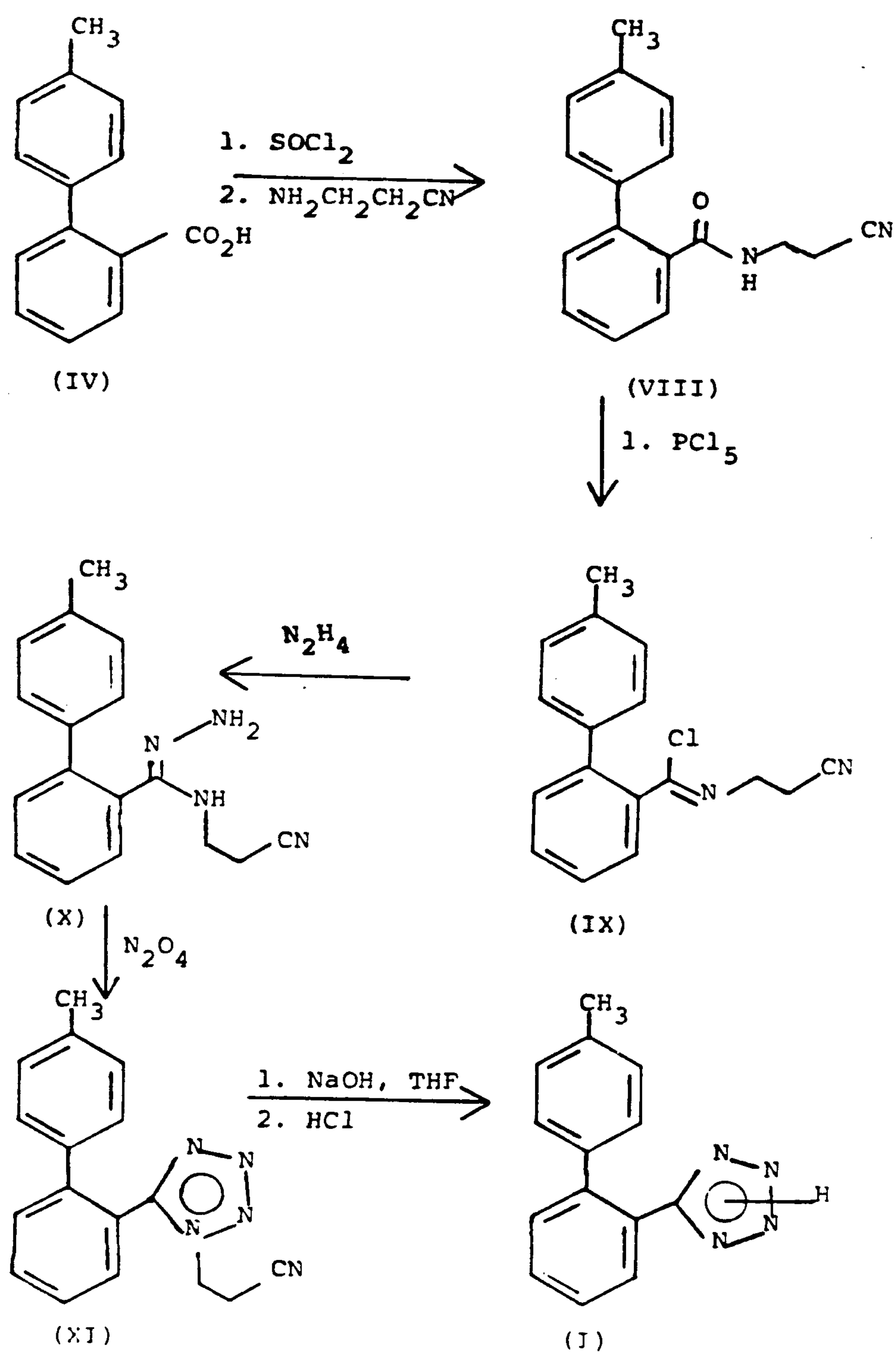
Scheme III



(I) (VII)

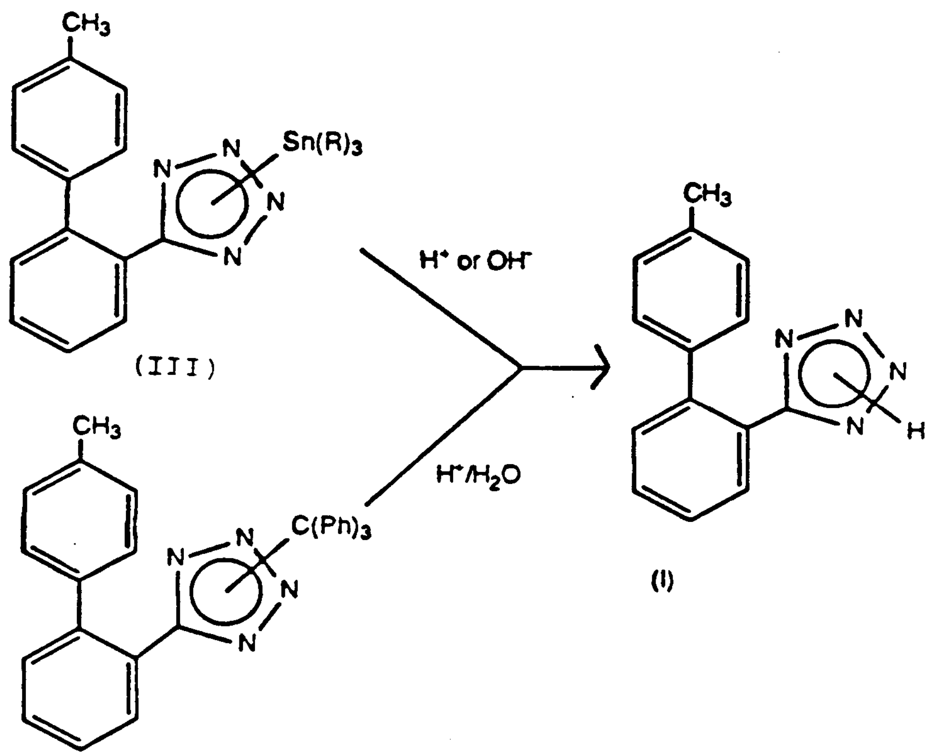
The propionitrile protecting group is attached as shown on Scheme IV. The biphenylcarboxylic acid (IV) may be converted to the acid chloride by a variety of reagents familiar to one skilled in the art. The intermediate acid chloride reacts with β-aminopropionitrile in the presence of an acid scavenger such as aqueous sodium hydroxide to yield amide (VIII). Amide (VIII) reacts with phosphorus pentachloride or phosgene to form the intermediate iminoyl chloride (IX) which when reacted with hydrazine yields amidrazone (X). The amidrazone (X) reacts readily with dinitrogen tetroxide (N_2O_4), which can be conveniently handled as a solution in carbon tetrachloride, to yield tetrazole (XI). Hydrazines and hydrazides have been shown to undergo facile conversion to their corresponding azides with N_2O_4 as described by Y.H. Kim, et. al., Tetrahedron Letters, 27, 4749(1986). The protected tetrazole (XI) is deprotected with aqueous base such as 1N NaOH with or without an additional organic solvent such as tetrahydrofuran to yield tetrazole (I). The amidrazone (X) may also be converted to the tetrazole (XI) using nitrous acid or its equivalents as described by D. G. Neilson, et. al., Chem. Rev., 70, 151(1970).

Scheme IV



Preferred protecting groups are those where X^1 is $Sn(R)_3$ and $C(Phenyl)_3$ and R is as described previously (Scheme V). The above groups may be optionally removed via acidic or basic hydrolysis, catalytic hydrogenation, and irradiation described by Greene, Protective Groups in Organic Synthesis, Wiley-Interscience, (1980).

Scheme V



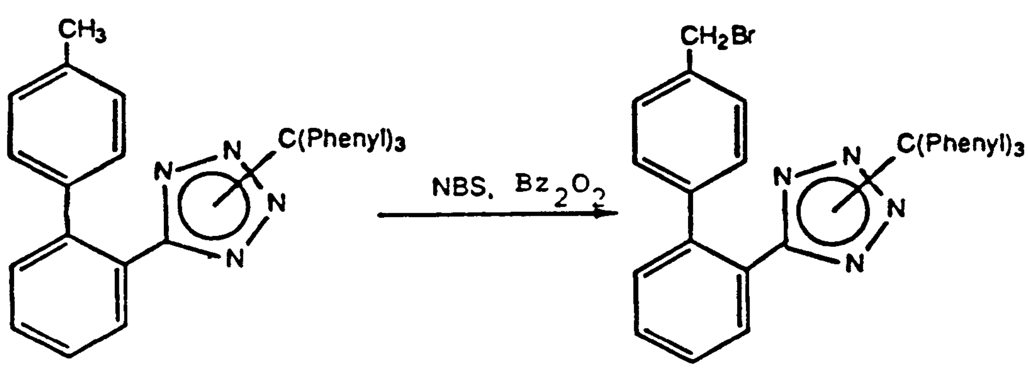
(III)

(VII)

(I)

Compounds of the Formula (I) where X^1 is C(phenyl)$_3$ and X^2 is Br may be prepared via radical bromination of (VII) with N-bromosuccinimide (NBS) and dibenzoylperoxide (Bz_2O_2) to yield (XII) as shown in Scheme VI. An example of this conversion is described by L. Horner et al., Angew. Chem., 71, 349 (1959).

Scheme VI

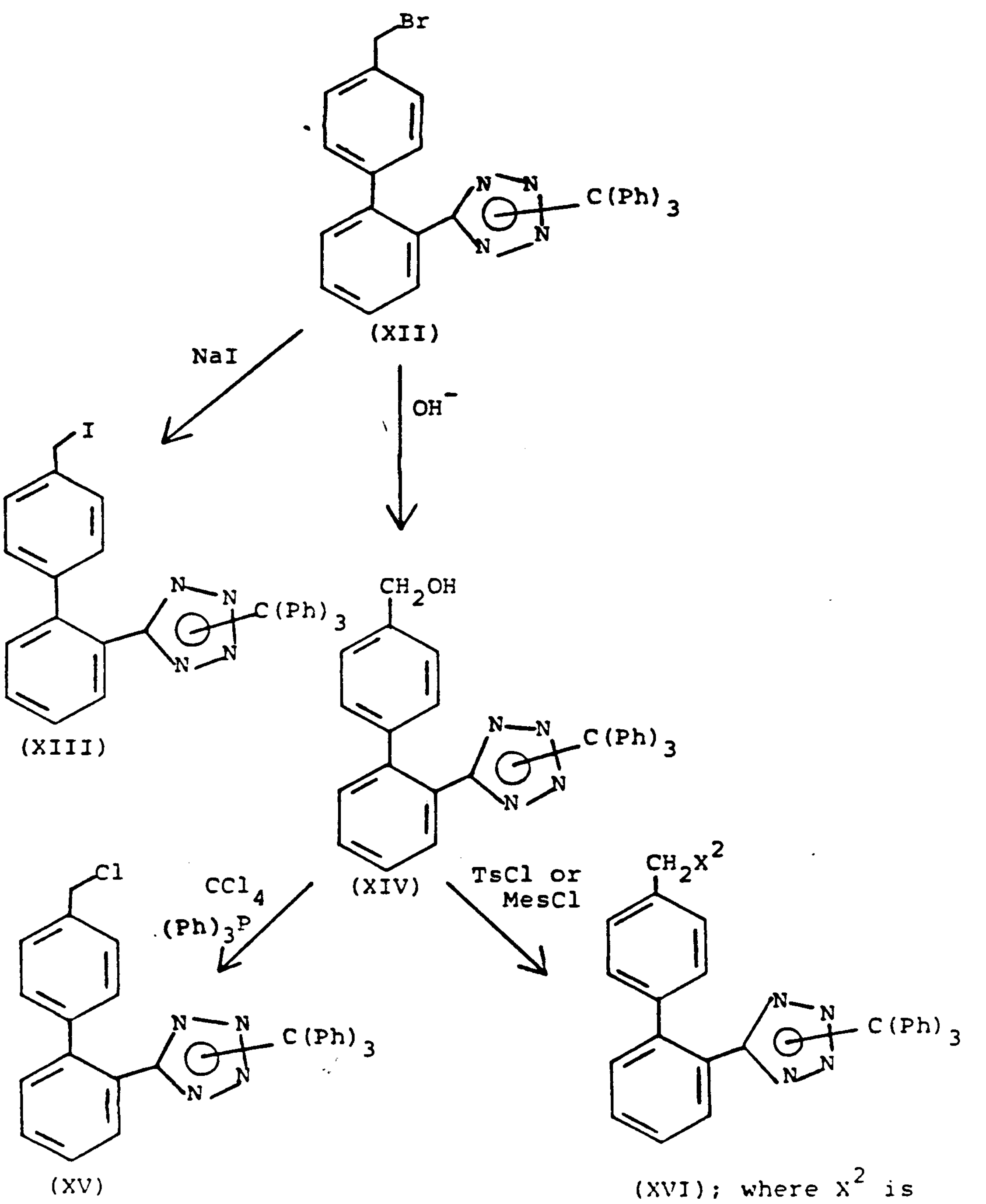


(VII)

(XII)

Compounds of the Formula (I) where X^1 is $C(Phenyl)_3$ and X^2 is I may be prepared via displacement of the bromine moiety in (XII) with sodium iodide in acetone under standard conditions yielding (XIII). Displacement of the above bromide (XII) with hydroxide ion affords the substituted benzyl alcohol (XIV). The benzyl alcohol (XIV) may be converted to the chloride (XV) via reaction with carbon tetrachloride and triphenylphosphine. The benzyl alcohol (XIV) can be converted to the tosylate or mesylate (XVI) via reaction with p-toluenesulfonyl chloride or methanesulfonyl chloride, respectively, in pyridine under standard conditions (Scheme VII).

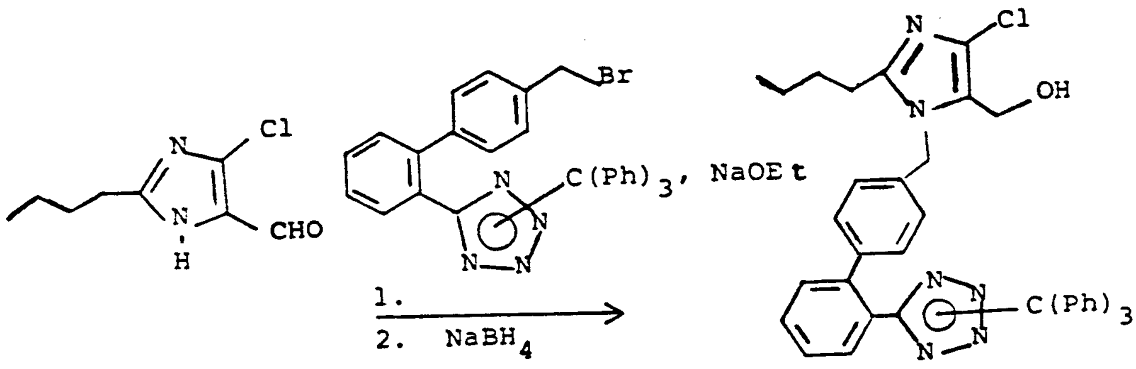
Scheme VII



(XVI); where X^2 is $OSO_2C_6H_4CH_3$ or OSO_2CH_3

Compounds of the Formula (I) where X^1 is $C(Phenyl)_3$ and X^2 is imidazoyl where R^1 is n-butyl, R^3 is Cl, and R^2 is hydroxymethyl may be prepared via alkylation of imidazole (XVII) with the appropriately substituted benzyl halide using sodium ethoxide as a base followed by reduction of the formaldehyde moiety on imidazole (XVII) to hydroxymethyl with sodium borohydride affording (XVIII). The preparation of imidazole (XVII) in Scheme VIII is described by Furukawa, et.al. in U.S. 4,355,040.

Scheme VIII



(XVII) (XVIII)

The compounds of this invention and their preparation can be understood further by the following examples. In these examples,unless otherwise indicated, all temperatures are in degrees centigrade and parts and percentages are by weight.

Example 1 - Method A

Part A: N-trimethylstannyl-5-[2-(4′-methylbiphen-2-yl)]tetrazole

To a solution of 2-cyano-4′-methylbiphenyl (19.30 g, 0.100 mole) in toluene (110.0 ml) was added trimethyltin azide (24.60 g, 0.120 mole) at room temperature. The reaction was refluxed for 24 hours, cooled to room temperature and the product isolated by filtration affording N-trimethylstannyl-5-[2-(4′-methylbiphenylyl)]tetrazole (32.60 g, 82%) as an off white solid, m.p. 265° (dec.); ^{1}H NMR (DMSO-d_6) δ: 7.50 (s,4H); 7.00 (s,4H); 2.25 (s,3H); 0.35 (s,3H).

Part B: 5-[2-(4′-methylbiphenylyl)]tetrazole (Compound not according to the invention)

To a solution of N-trimethylstannyl-5-[2-(4′-methylbiphenylyl)]tetrazole (32.0 g, 0.080 mole) in toluene (230 ml) and tetrahydrofuran (15.0 ml) was bubbled in enough anhydrous hydrogen chloride to give a clear solution at room temperature. From this solution, 5-[2-(4′-methylbiphenylyl)]tetrazole (19.1 g) crystallized. Recrystallization from toluene afforded 18.1 g (95%) of product, m.p. 149-152°. ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ: 7.50 (m,4H); 7.07 (m,4H); 2.35 (s,3H).

Example 1 - Method B

Part A: 4′-Methyl-biphenyl-2-carbonyl chloride

A solution of 4′-methyl-biphenyl-2-carboxylic acid (31.84g, 0.15 mole) in chloroform (200 ml) was added dropwise to a stirred mixture of chloroform (25ml) oxalyl chloride (25ml), and dimethylformamide (1.0ml) at room temperature. After the mixture had stirred for 24 hours at room temperature, the solution was evaporated in vacuo affording 36.4 grams of the crude acid chloride. IR: 1784.0 cm $^{-1}$(COCl).

Part B: N-(4-Nitrobenzyl)-4′-methyl-biphenyl-2-carboxamide

A solution of the material from Part A (36.4 g) in dry acetonitrile was added dropwise to a cooled (ice-bath), stirred mixture of 4-nitrobenzylamine hydrochloride (23.45 g, 0.12 mole), 4-dimethylamino pyridine (0.5g, 0.0041 mole), and dry pyridine (150.0 ml). After 30 minutes, the reaction was allowed to reach room temperature and stirred for 16 hours at room temperature. The mixture was poured into a stirred mixture of 3N HCl (800.0 ml), ice (400.0 g), and dichloromethane (400 ml). The organic layer was washed with 2N

NaOH (2 x 200 ml), brine (100 ml), dried ($MgSO_4$), and evaporated in vacuo to yield crude product (61.9g). Recrystallization from ethyl acetate gave 31.3 (73%) of product, m.p. 153-154°. ^1H NMR ($CDCl_3$) δ: 8.03 (d, 2H, aromatic); 7.65-7.69 (m, 1H, aromatic); 7.12-7.48 (m, 7H, aromatic); 7.04 (d, 2H, aromatic); 5.77-5.79 (m, 1H, NH); 4.41 (d, 2H, J = 6.0 Hz, CH_2); 2.39 (s, 3H, CH_3). Mass spec m/z = 347 (M + 1).

Part C: N-(4-Nitrobenzyl)-4′-methyl-biphen-2-yl-carboiminoyl chloride

In three portions, a total of 20.78g (0.060 mole) of the product of Part B was added to a cooled (ice-bath), stirred solution of phosphorus pentachloride (12.49 g, 0.066 mole) in carbon tetrachloride (200 ml). The mixture was stirred for 30 minutes at 0°, allowed to warm to room temperature, and stirred for 16 hours. The mixture was evaporated in vacuo yielding the crude product (21.3g). IR: 1691 cm^{-1} (C=N). ^1H NMR ($CDCl_3$) δ: 4.79 (s, 2H, CH_2).

Part D: 1-(4-Nitrobenzyl)-5-(4′-methyl-biphen-2-yl) tetrazole

Lithium azide (3.67g, 0.75 mole) was added portionwise to a cooled solution (ice-bath) of the product of Part C (21.3g) in dimethylformamide (200.0 ml). The mixture was allowed to reach room temperature over 16 hrs. The reaction mixture was evaporated in vacuo. The residue was partitioned between water and ethyl acetate (100 ml). The organic layer was washed with water (100 ml), dried ($MgSO_4$) and evaporated in vacuo to yield 19.5 g of a dark residue. Chromatography on silica ($CHCl_3$) followed by recrystallization (methanol) afforded 5.37 g, (24.1%), m.p. 95.0-96.0°. ^1H NMR ($CDCl_3$) δ: 7.98-8.02 (m, 2H, aromatic); 7.55-7.70 (m, 2H, aromatic); 7.37-7.49 (m, 2H, aromatic); 6.99-7.10 (m, 2H, aromatic); 4.87 (d, J=8.7 Hz, aromatic); 4.88 (s, 2H, CH_2); 2.33 (s, 3H, CH_3). Mass spec m/z = 372 (M + 1).

Part E: 5-[2-(4′-methylbiphen-2-yl)]tetrazole(Compound not according to the invention)

A mixture of the product of Part D (1.00 g, 2.80 mmole), ethanol (150.0 ml), and W6 Raney nickel (5.0 g) was hydrogenated in a Parr® Shaker at 50 psi for 2 hrs. at room temperature. The catalyst was removed by filtration, and the filtrate was evaporated in vacuo. The residue was partitioned between water and diethyl ether (100 ml) and the organic layer was washed with 1N HCl (50 ml), brine (50 ml), dried ($MgSO_4$), and evaporated in vacuo to yield a solid residue which was recrystallized from toluene to yield the product (0.19 g, 28.7%), m.p. 154-155°. ^1H NMR ($CDCl_3$) δ; 11.5 (br s, 1H, NH); 8.02 (d, 1H, aromatic); 7.38-7.61 (m, 3H, aromatic), 7.16 (d, 2H, J=8.0 Hz, aromatic); 7.04 (d, 2H, J=8.0 Hz); 2.35 (s, 3H, CH_3). Mass spec m/z=237 (M + 1).

Example 1 - Method C

Part A: 2-(β-cyanoethylaminocarbonyl)-4′-methylbiphenyl

4′-methylbiphenyl-2-carboxylic acid (50.00 g, 0.236 mol,), thionyl chloride (87.5 ml, 1.20 mol) and chloroform (500 ml) were mixed and refluxed for 4 hours. The thionyl chloride and solvent were removed in vacuo, and the residue suspended in toluene (300 ml). The mixture was evaporated in vacuo and the residue suspended once more in toluene and evaporated to insure removal of traces of thionyl chloride. The resultant acid chloride was dissolved in tetrahydrofuran (100 ml) and slowly added in five equal portions alternatingly with five equal portions of 1,0N NaOH (236.0 ml, 0.236 mol) to a solution of β-aminopropionitrile fumarate (30.3 g, 0.236 mol) in 1,0 N NaOH (236.0 ml, 0.236 mol) at 0° with stirring. The reaction was allowed to warm slowly to room temperature. After 24 hrs, water (500 ml) was added and the aqueous mixture extracted with ethyl acetate (3 x 500 ml). The organic layers were combined and dried ($MgSO_4$), and the solvent removed in vacuo to yield a crude solid which, after recrystallization from methylcyclohexane/butyl chloride, yielded 53.5 g of a white solid. M.P. = 102.0-103.5°. NMR (200MH$_2$, $CDCl_3$) δ:7.68 (d, 1H, J=7H$_z$); 7.56-7.19 (m, 7H); 5.65 (bm, 1H); 3.43 (d of t, 2H); 2.39 (t, 2H, J=7H$_z$). Anal. calcd. for $C_{17}H_{16}N_2O$; C, 77.25; H, 61.0; N, 10.60. Found; C, 77.42; H, 6.40; N, 10.68.

Part B: N^3-(β-cyanoethyl)-4′-methylbiphenyl-2-yl-amidrazone.

2-(β-cyanoethylaminocarbonyl)-4′-methylbiphenyl (33.48g, 0.127 mol) and phosphorous pentachloride (28.01g, 0.139 mol) were combined in a round bottom flask which was then connected to aspirator vacuum via a trap filled with calcium chloride. The flask was gently heated with a heat gun until the solids melted.

The flask was intermittantly heated for 15-20 minutes.

The crude iminoyl chloride was taken up in dry dioxane (100 mL) and added dropwise to a stirred mixture of hydrazine (20.1 mL, 0.634 mol) in dry dioxane (200 mL). After 24 hours, the excess hydrazine and solvent were removed in vacuo. Water (300 mL) was added, and the aqueous mixture extracted with ethyl acetate (3 x 300 mL). The organic layers were combined, dried ($MgSO_4$) and the solvent removed in vacuo to yield an oil. The oil was treated with a 1:1 hexane/ethyl acetate solution (30-50 mL), and solids precipitated. These were collected and dried to yield 16.14g of light pink solids. M.P. = 146.5-147.5°. Chemical ionization mass spectrum detected $(M+H)^+$ = 279 for $C_{17}H_{19}N_4$. Anal. calcl. for $C_{17}H_{18}N_4 \bullet (N_2H_4)_{0.1}$: C, 72.52; H, 6.44; N, 20.89. Found: C, 72.50; H, 6.54; N,21.13. NMR indicated a mixture of tautomeric forms.

Part C: 2-[1-(β-cyanoethyl)-1-H-tetrazol-5-yl]-4′-methylbiphenyl.

A solution of N_2O_4(g) in carbon tetrachloride (0.73M, 19.6 mL, 14.3mmol) was added to a stirred slurry of $N^{\underline{3}}$(β-cyanoethyl)-4′-methylbiphenyl-2-ylamidrazone (2.00g, 7.2mmol) in anhydrous acetonitrile (40 mL) at 0°. The reaction was warmed to room temperature and stirred overnight. The solvent was removed in vacuo to yield a crude solid. This solid was taken up in butyl chloride and the insoluble matter filtered. The filtrate was evaporated, and the residue flash chromatographed on silica in 1:1 hexane/ethylacetate to yield 1.10g of a pale yellow oil, which slowly crystallized. Recrystallization from hexane/butyl chloride yielded 910 mg of pale yellow crystals. M.P. = 90.0-92.0°. NMR(200 MH_z, $CDCl_3$) δ: 7.76-7.50 (m,4H); 7,17(d, 2H, J=10H_z); 7.04(d,2H, J=10H_z); 3.80 (t,2H, J=7H_z); 2.37 (s,3H); 2.24(bt, 2H, J=7H_z). Anal. calcd. for $C_{17}H_{15}N_5$: C, 70.57; H,5.23; N,24.20. Found: C, 70.49; H, 5.45; N, 24.44.

Part D: 5-(4′-methylbiphenyl-2-yl)tetrazole (Compound not according to the invention)

2-[1-(β-cyanoethyl)-1-H-tetrazol-5-yl]-4′-methylbiphenyl (689mg, 2.38 mmol), 1,0N NaOH (2.62 mL), 2.62 mmol) and THF (15 mL) were mixed and stirred at room temperature. After 15 minutes, water (100 mL) was added and the pH adjusted to 3.0 with conc. HCl. The aqueous mixture was extracted with ethyl acetate (3 x 100 mL) and the organic layers were combined, dried ($MgSO_4$) and evaporated in vacuo to yield 550 mg of a white powder. M.P. = 148.5-150.0°. The spectral data matched those of a sample prepared via Method A.

Example 5

N-triphenylmethyl-5-[2-(4′-methylbiphenylyl)]tetrazole (Compound not according to the invention)

To a solution of 5-[2-(4′-methylbiphenyl)] tetrazole (17.0 g, 0.072 mole) in methylene chloride (260 ml) was added triphenylmethyl chloride (21.20 g, 0.076 mole) at room temperature. Triethylamine (12.0 ml, 0.086 mole) was added at room temperature, and the solution was refluxed for 2.5 hrs. The solution was cooled to room temperature, washed with water (2 x 50 ml), dried ($MgSO_4$), and evaporated in vacuo. The residue was crystallized from toluene (80 ml), yielding, N-triphenylmethyl-5-[2-(4′-methylbiphenylyl)]tetrazole (31.2 g, 90%), m.p. 163-166°; ^1H NMR ($CDCl_3$) δ: 8.10-6.80 (complex, 23H); 2.28 (s, 3H).

Example 6

N-triphenylmethyl-5-[2-(4′-bromomethyl-biphenylyl)] tetrazole

To a solution of N-triphenylmethyl-5-[2-(4′-methylbiphenylyl)]tetrazole (31.0 g, 0.065 mole) in carbon tetrachloride (390.0 ml) was added N-bromosuccinimide (11.50 g, 0.065 mole) and dibenzoylperoxide (1.10 g, 0.0045 mole) at room temperature. The reaction mixture was refluxed for 3 hrs., cooled to 40° and filtered. Evaporation of the filtrate in vacuo followed by trituration of the residue with isopropyl ether (100.0 ml) yielded N-triphenylmethyl-5-[2-(4′-bromomethyl-biphenylyl)]tetrazole (33.10 g, 92%), m.p. 135-138°. ^1H NMR ($CDCl_3$) δ: 8.20-6.70 (complex, 23H); 4.33 (s, 2H).

Example 7

1-{[2′-(N-triphenylmethyl-tetrazol-5-yl)-biphenyl-4-yl] methyl}-2-butyl-4-chloro-5-hydroxymethyl imidazole

To a solution of 2-butyl-4-chloro-5-formyl-imidazole (1.24 g, 0.007 mole) dissolved in dimethylformamide (10.0 ml) was added sodium ethoxide (0.45 g, 0.0066 mole) and the reaction mixture was cooled to 5°. N-triphenylmethyl-5-[2-(4′-bromomethylbiphenylyl]tetrazole (3.70 g, 0.0066 mole) was added and the reaction mixture was allowed to warm to room temperature. After 72 hrs. the reaction was diluted with water (25.0 ml) and extracted with ethyl acetate (3 x 25 ml). The organic phase was washed with water (2 x 25 ml) and brine (3 x 25 ml), dried ($MgSO_4$), and evaporated in vacuo to an oil. The crude oil was dissolved in methanol (20.0 ml), and sodium borohydride (0.24 g, 0.0063 mole) was added at room temperature. The reaction was stirred for 1.5 hrs., diluted with water (40.0 ml), and extracted with ethyl acetate (2 x 50 ml). The organic layer was washed with water (1 x 25 ml), dried ($MgSO_4$), and evaporated in vacuo. The residue was recrystallized once from toluene/heptane, once from toluene, and finally from methanol to give 1-{[2′-(N-triphenylmethyl-tetrazol-5-y)}-biphenyl-4-yl] methyl}-2-butyl-4-chloro-5-hydroxymethyl imidazole (0.98 g, 21%), m.p. 95-98°; ^{1}H NMR ($CDCl_3$) δ: 8.20- 6.60 (complex, 23H); 5.16 (s, 3H); 4.40 (s, 3H); 2.85 (brs, 1H); 2.54 (t, 3H); 1.9-1.1 (m, 4H); 0.88 (t, 3H).

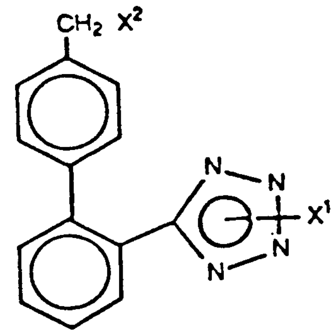
Example 8

1-{[2′-(N-trimethylstannyl-tetrazol-5-yl)-biphenyl-4-yl] methyl}-2-butyl-4-chloro-5-hydroxymethyl imidazole

To a solution of 1-[(2′-cyano-biphenyl-4-yl) methyl]-2-butyl-4-chloro-5-hydroxymethyl-imidazole (4.40 g, 0.011 mole) in xylenes (40.0 ml) was added trimethyltin azide (2.80 g, 0.014 mole), and the reaction was heated at 115-120° for 40 hrs. The mixture was cooled to 50° and filtered to yield 1-{[2′-(N-trimethylstannyl-tetrazol-5-yl)-biphenyl-4-yl] methyl}-2-butyl-4-chloro-5-hydroxymethyl imidazole (6.55 g, 99%), m.p. 154-160°; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ: 7.80-7.30 (m, 4H), 7.03 (q, 4H), 5.23 (s, 3H), 4.43 (s, 3H), 2.54 (t, 3H); 2.00 (s, 1H), 1.80-1.10 (m, 4H); 0.85 (t, 3H); 0.40 (s, 9H).

The compounds of Examples 1,5,6,7, and 8 above as well as other compounds which were prepared or could be prepared using the procedures of the aforementioned examples are shown in Table I.

TABLE I



Ex.	X^1	X^2	Method	R^1	R^2	R^3	M.P.°C
1	H	H	A,B,C	-	-	-	149-155
1D	P-NO_2benzyl	H	B	-	-	-	95-96
2	$Sn(Ph)_3$	H	A	-	-	-	204-209
3	Sn(n-Pr)$_3$	H	A	-	-	-	-
4	$Sn(c\text{-}C_6H_{11})_3$	H	A	-	-	-	-
5	C(Phenyl)$_3$	H	-	-	-	-	163-166
6	C(Phenyl)$_3$	Br	-	-	-	-	135-138
7	C(Phenyl)$_3$	Im	-	n-Bu	CH_2OH	Cl	95-98
8	$Sn(CH_3)_3$	Im	A	n-Bu	CH_2OH	Cl	154-160
9	$Sn(Ph)_3$	Im	A	n-Bu	CH_2OH	Cl	
10	Sn(n-Bu)$_3$	Im	A	n-Bu	CH_2OH	Cl	

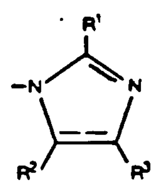
(note: the compounds of Ex. 1 to 5 are not according to the invention)

TABLE I (continued)

Ex.	X^1	X^2	Method	R^1	R^2	R^3	M.P.°C
11	H	OH	-	-	-	-	
12	C(Phenyl)$_3$	Cl	-	-	-	-	
13	Sn(CH_3)$_3$	Im	A	n-Pr	CH_2OH	Cl	
14	Sn(Ph)$_3$	Im	A	n-Pr	CH_2OH	Cl	
15	Sn(n-Bu)$_3$	Im	A	n-Pr	CH_2OH	Cl	
16	C(Phenyl)$_3$	Im	-	n-Pr	CH_2OH	Cl	
17	p-$NO_2C_6H_4CH_2$	Im	B	n-Bu	CH_2OH	Cl	
18	Sn(CH_3)$_3$	Im	A	n-Bu	CHO	Cl	
19	C(Phenyl)$_3$	Im	-	n-Bu	CHO	H	
20	Sn(CH_3)$_3$	Im	A	n-Bu	$CH_2NHCO_2CH_3$	Cl	
21	Sn(CH_3)$_3$	Im	A	n-Bu	$CH_2NHSO_2CH_3$	Cl	
22	C(Phenyl)$_3$	Im	-	n-Bu	$(CH_2)_3O-\overset{O}{\overset{\|\|}{C}}-CH_3$	Cl	
23	Sn(CH_3)$_3$	Im	A	n-Bu	$CH_2NHSO_2CF_3$	Cl	
24	C(Phenyl)$_3$	Im	A	n-Bu	$CH_2NHSO_2CF_3$	Cl	
25	Sn(CH_3)$_3$	Im	A	n-Bu	CH_2OH	H	
26	C(Ph)$_3$	Im	-	n-Bu	CH_2OH	H	
27	Sn(CH_3)$_3$	Im	A	n-Bu	CHO	H	
28	C(Ph)$_3$	Im	-	n-Bu	CHO	H	
29	Sn(CH_3)$_3$	Im	A	$-CH=CHCH_3$	CH_2OH	Cl	

TABLE 1 (continued)

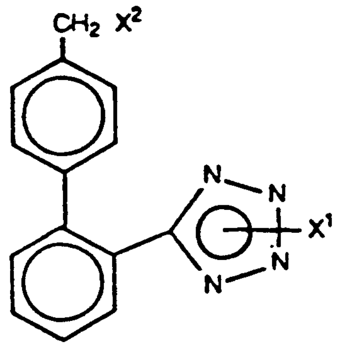
Ex.	X^1	X^2	Method	R^1	R^2	R^3	M.P.°C
30	$C(Ph)_3$	Im	-	$-CH{=}CHCH_3$	CH_2OH	Cl	
31	$Sn(CH_3)_3$	Im	A	$-C{\equiv}C{-}CH_3$	CH_2OH	Cl	
32	$C(Ph)_3$	Im	-	$-C{\equiv}C{-}CH_3$	CH_2OH	Cl	
33	CH_2CH_2CN	Im	C	n-Bu	CH_2OH	Cl	
34	$C(Phenyl)_3$	I	-	-	-	-	
35	$C(Phenyl)_3$	OTs	-	-	-	-	
36	$C(Phenyl)_3$	OMes	-	-	-	-	
37	$Sn(CH_3)_3$	OH	A	-	-	-	
38	$Sn(Ph)_3$	OH	A	-	-	-	
39	$Sn(c\text{-}C_6H_{11})_3$	OH	A	-	-	-	

Im =  ;

Claims

Claims for the following Contracting States : AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE

1. A tetrazole having the formula:

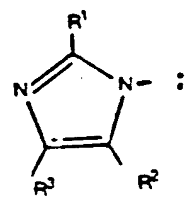


(I)

wherein

X^1 is H, $Sn(R)_3$, -C(Phenyl)$_3$, p-nitrobenzyl, or β-propionitrile.

X^2 is Cl, Br, I, O-tosyl, OH, O-mesyl, or



R is alkyl of 1-6 carbon atoms, phenyl or cyclohexyl;

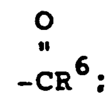
R^1 is alkyl of 3-10 carbon atoms, alkenyl of 3 to 10 carbon atoms, alkynyl of 3 to 10 carbon atoms, and benzyl substituted with up to two groups selected from alkoxy of 1 to 4 carbon atoms, halogen, alkyl of 1 to 4 carbon atoms, nitro and amino:

R^2 is phenylalkenyl wherein the aliphatic portion is 2 to 4 carbon atoms, $-(CH_2)_m$-imidazoyl-1-yl, $-(CH_2)_m$-1,2,3-triazolyl optionally substituted with one or two groups selected from CO_2CH_3 and alkyl of 1 to 4 carbon atoms, $(CH_2)_m$-tetrazolyl, $-(CH_2)_nOR^4$;

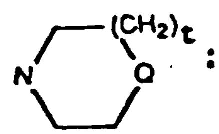
$$-(CH_2)_nO\overset{O}{\overset{\|}{C}}R^5;\quad -CH{=}CH(CH_2)_s\overset{O}{\overset{\|}{C}}R^6;$$

$$-CH{=}CH(CH_2)_s\underset{R^5}{\underset{|}{C}}HOR^7;\quad -(CH_2)_n\overset{O}{\overset{\|}{C}}R^6;\quad -(CH_2)_nNH\overset{O}{\overset{\|}{C}}-OR^8;$$

$-(CH_2)_nNHSO_2R^8$; $-(CH_2)_mF$;

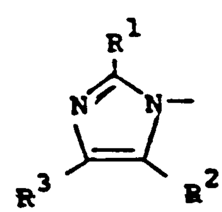


R^3	is H, F, Cl, Br, I, NO_2, CF_3, or CN;
R^4	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl or benzyl;
R^5	is H, alkyl or perfluoroalkyl of 1 to 8 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl or benzyl;
R^6	is H, alkyl of 1-5 carbon atoms, OR^9 or $NR^{10}R^{11}$;
R^7	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl, benzyl, acyl of 1 to 4 carbon atoms, phenacyl;
R^8	is alkyl of 1 to 6 carbon atoms or perfluoroalkyl of 1 to 6 carbon atoms, 1-adamantyl, 1-naphthyl, 1-(1-naphthyl)ethyl, or $(CH_2)_pC_6H_5$;
R^9	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, or phenyl;
R^{10} and R^{11}	independently are H, alkyl of 1 to 4 carbon atoms, phenyl, benzyl or taken together to form a ring of the Formula



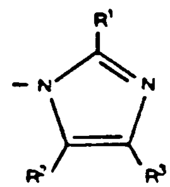
Q	is NR^{12}, O, or CH_2;
R^{12}	is H, alkyl of 1 to 4 carbon atoms, or phenyl;
m	is 1 to 5;
n	is 1 to 10;
s	is 0 to 5;
p	is 0 to 3;
t	is 0 or 1.

with the proviso that when X^1 = H then X^2 cannot be



2. The tetrazole of Claim 1 wherein X^1 is H, $Sn(R)_3$ or -C(Phenyl)$_3$ where R is alkyl of 1 to 6 carbon atoms or phenyl.

3. The tetrazole of Claim 1 wherein X^2 is Br, Cl or



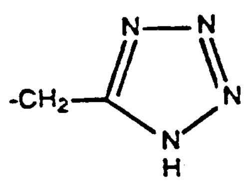
where R^1, R^2 and R^3 are as defined in Claim 1.

4. The tetrazole of Claim 3 wherein
   - R^1 is alkyl, alkenyl or alkynyl of 3 to 7 carbon atoms;
   - R^2 is $-(CH_2)_mOR^4$;

$$-(CH_2)_mO\overset{O}{\overset{\|}{C}}R^5;\quad -CH{=}CH{-}\overset{R^5}{\overset{|}{C}}HOR^7$$

$$-(CH_2)_m\overset{O}{\overset{\|}{C}}{-}R^6;\quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8;$$

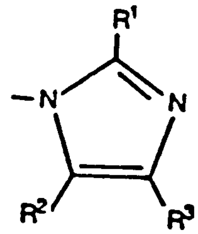
$-(CH_2)_mNHSO_2R^8$;



$; \text{ or } -\overset{O}{\overset{\|}{C}}R^6; \;;$

   - R^3 is H, Cl, Br, or I;
   - R^4 is H, or alkyl of 1 to 4 carbon atoms;
   - R^5 is H, or alkyl of 1 to 4 carbon atoms;
   - R^6 is H, alkyl of 1 to 5 carbon atoms; OR^9; or $NR^{10}R^{11}$;
   - R^7 is H, alkyl of 1 to 4 carbon atoms, or acyl of 1 to 4 carbon atoms;
   - R^8 is CF_3, alkyl of 1 to 6 carbon atoms or phenyl;
   - m is 1 to 5.

5. The tetrazole of Claim 1 wherein X^1 is H, $Sn(R_3)$ or $-C(Phenyl)_3$ where R is alkyl of 1 to 6 carbon atoms or phenyl, and X^2 is Br, Cl or



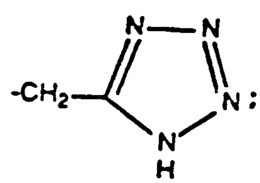
where R^1 is alkyl, alkenyl or alkynyl of 3 to 7 carbon atoms;

R^2 is $-(CH_2)_mOR^4$;

$$-(CH_2)_mO\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH-\overset{R^5}{\overset{|}{C}H}OR^7$$

$$-(CH_2)_m\overset{O}{\overset{\|}{C}}-R^6; \quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8;$$

$-(CH_2)_mNHSO_2R^8$;

 ; or $-\overset{O}{\overset{\|}{C}}R^6$;

R^3 is H, Cl, Br, or I;

R^4 is H, or alkyl of 1 to 4 carbon atoms;

R^5 is H, or alkyl of 1 to 4 carbon atoms;

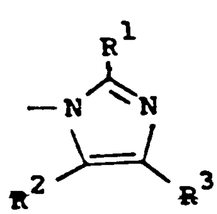
R^6 is H, alkyl of 1 to 5 carbon atoms; OR^9; or $NR^{10}R^{11}$;

R^7 is H, alkyl of 1 to 4 carbon atoms, or acyl of 1 to 4 carbon atoms;

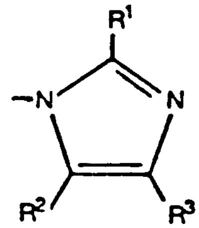
R^8 is CF_3, alkyl of 1 to 6 carbon atoms or phenyl;

m is 1 to 5.

with the proviso that when X^1 = H then X^2 is not



6. The tetrazole of Claim 5 wherein X^2 is Br or



wherein

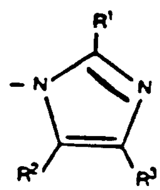
R^1 is alkyl of 3 to 7 carbon atoms;

R^2 is $-(CH_2)_mOR^4$ where m is 1 to 5 and R^4 is H or alkyl of 1 to 4 carbon atoms; and

R^3 is Cl.

7. The tetrazole of Claim 6 wherein X^2 is Br.

8. The tetrazole of Claim 6 wherein X^2 is



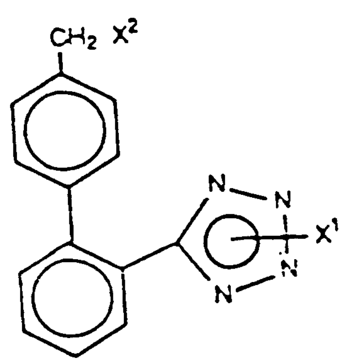
;

wherein R^1, R^2 and R^3 are as defined in Claim 6.

9. The tetrazole of Claim 8 wherein R^1 is n-butyl, R^2 is $-CH_2OH$ and R^3 is Cl.

Claims for the following Contracting State : ES

1. Process for the production of a tetrazole having the formula :

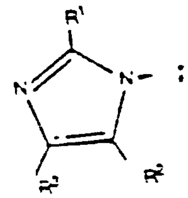


(I)

wherein

X^1 is H, $Sn(R)_3$, $-C(Phenyl)_3$, p-nitrobenzyl, or β-propionitrile.

X^2 is Cl, Br, I, O-tosyl, OH, O-mesyl, or



R	is alkyl of 1-6 carbon atoms, phenyl or cyclohexyl;
R^1	is alkyl of 3-10 carbon atoms, alkenyl of 3 to 10 carbon atoms, alkynyl of 3 to 10 carbon atoms, and benzyl substituted with up to two groups selected from alkoxy of 1 to 4 carbon atoms, halogen, alkyl of 1 to 4 carbon atoms, nitro and amino;
R^2	is phenylalkenyl wherein the aliphatic portion is 2 to 4 carbon atoms, $-(CH_2)_m$-imidazoyl-1-yl, $-(CH_2)_m$-1,2,3-triazolyl optionally substituted with one or two groups selected from CO_2CH_3 and alkyl of 1 to 4 carbon atoms, $(CH_2)_m$-tetrazolyl, $-(CH_2)_nOR^4$;

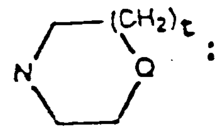
$$-(CH_2)_n O\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH(CH_2)_s\overset{O}{\overset{\|}{C}}R^6;$$

$$-CH{=}CH(CH_2)_s\underset{R^5}{\underset{|}{C}}HOR^7; \quad -(CH_2)_n\overset{O}{\overset{\|}{C}}R^6; \quad -(CH_2)_nNH\overset{O}{\overset{\|}{C}}-OR^8;$$

$-(CH_2)_nNHSO_2R^8$; $-(CH_2)_mF$;

$$-\overset{O}{\overset{\|}{C}}R^6;$$

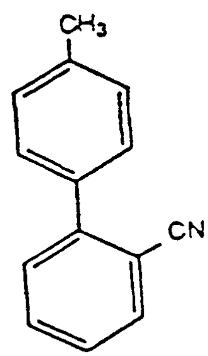
R^3	is H, F, Cl, Br, I, NO_2, CF_3, or CN;
R^4	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl or benzyl;
R^5	is H, alkyl or perfluoroalkyl of 1 to 8 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl or benzyl;
R^6	is H, alkyl of 1-5 carbon atoms, OR^9 or $NR^{10}R^{11}$;
R^7	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, phenyl, benzyl, acyl of 1 to 4 carbon atoms, phenacyl;
R^8	is alkyl of 1 to 6 carbon atoms or perfluoroalkyl of 1 to 6 carbon atoms, 1-adamantyl, 1-naphthyl, 1-(1-naphthyl)ethyl, or $(CH_2)_pC_6H_5$;
R^9	is H, alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 6 carbon atoms, or phenyl;
R^{10} and R^{11}	independently are H, alkyl of 1 to 4 carbon atoms, phenyl, benzyl or taken together to form a ring of the Formula



Q	is NR^{12}, O, or CH_2;
R^{12}	is H, alkyl of 1 to 4 carbon atoms, or phenyl;
m	is 1 to 5;
n	is 1 to 10;
s	is 0 to 5:
p	is 0 to 3;
t	is 0 or 1

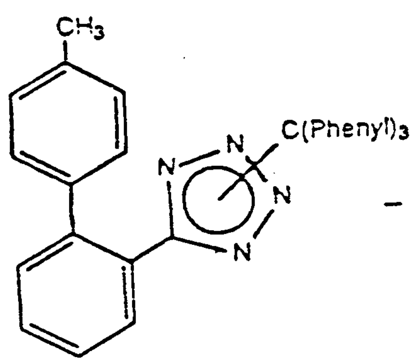
whereby

a) compounds of the Formula (I), where X^1 is $Sn(R)_3$ and R is alkyl of 1 to 6 carbon atoms or phenyl and X^2 is imidazoyl where R^1 is n-butyl, R^3 is Cl, and R^2 is hydroxymethyl may be prepared by the 1,3-dipolar cycloaddition of trialkyltin or triphenyltin azides to the appropriately substituted nitrile (II)



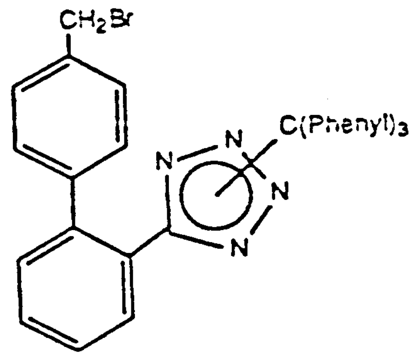
(II)

b) compounds of the Formula (I) where X^1 is C(phenyl)$_3$ and X^2 is Br may be prepared via radical bromination of (VII) with N-bromosuccinimide (NBS) and dibenzoylperoxide (Bz_2O_2)



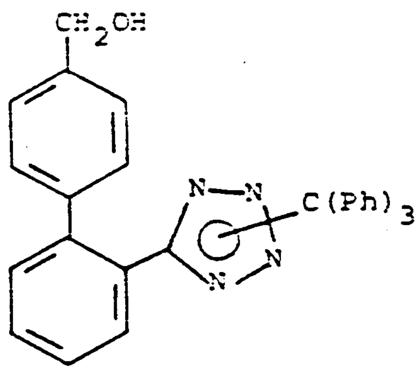
(VII)

c)compounds of the Formula (I) where X^1 is $C(Phenyl)_3$ and X^2 is I may be prepared via displacement of the bromine moiety in (XII) with sodium iodide in acetone under standard conditions



(XII)

d) compounds of the Formula (I) where X^1 is $C(Phenyl)_3$ and X^2 is OH may be afforded by a displacement-reaction of the bromide in Formula (XII) with a hydroxide ion;
e) compounds of the Formula (I) where X^1 is $C(Phenyl)_3$ and X^2 is the chloride can be afforded by reaction of the alcohol (XIV)

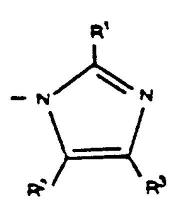


(XIV)

with carbontetrachloride and triphenylphosphine;
f) compounds of the Formula (I) where X^1 is $C(Phenyl)_3$ and X^2 is tosylate or mesylate can be afforded by reaction of the alcohol (XIV) with p-toluenesulfonyl chloride or methanesulfonyl chloride, respectively in pyridine under standard conditions;

2. The process of Claim 1 wherein X^1 is H, $Sn(R)_3$ or $-C(Phenyl)_3$ where R is alkyl of 1 to 6 carbon atoms or phenyl.

3. The process of Claim 1 wherein X^2 is Br, Cl or



where R^1, R^2 and R^3 are as defined in Claim 1.

4. The process of Claim 3 wherein

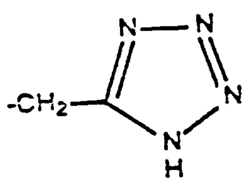
R^1 is alkyl, alkenyl or alkynyl of 3 to 7 carbon atoms;

R^2 is $-(CH_2)_mOR^4$;

$$-(CH_2)_mO\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH-\overset{R^5}{\overset{|}{C}}HOR^7$$

$$-(CH_2)_m\overset{O}{\overset{\|}{C}}-R^6; \quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8;$$

$-(CH_2)_mNHSO_2R^8$;

 ; or $-\overset{O}{\overset{\|}{C}}R^6$; ;

R^3 is H, Cl, Br, or I;

R^4 is H, or alkyl of 1 to 4 carbon atoms;

R^5 is H, or alkyl of 1 to 4 carbon atoms;

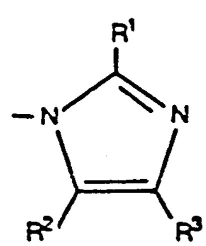
R^6 is H, alkyl of 1 to 5 carbon atoms; OR^9; or $NR^{10}R^{11}$;

R^7 is H, alkyl of 1 to 4 carbon atoms, or acyl of 1 to 4 carbon atoms;

R^8 is CF_3, alkyl of 1 to 6 carbon atoms or phenyl;

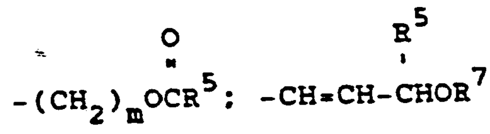
m is 1 to 5.

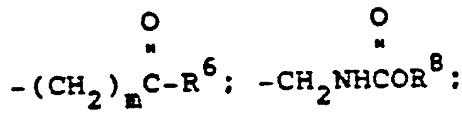
5. The process of Claim 1 wherein X^1 is H, $Sn(R_3)$ or -C(Phenyl)$_3$ where R is alkyl of 1 to 6 carbon atoms or phenyl, and X^2 is Br, Cl or



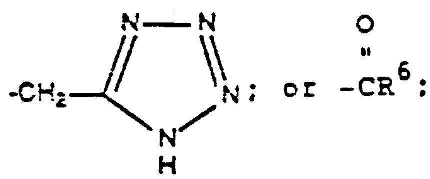
where R^1 is alkyl, alkenyl or alkynyl of 3 to 7 carbon atoms;

R^2 is $-(CH_2)_mOR^4$;



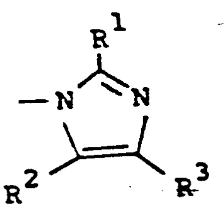


$-(CH_2)_mNHSO_2R^8$;

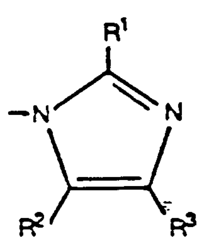


R^3 is H, Cl, Br, or I;
R^4 is H, or alkyl of 1 to 4 carbon atoms;
R^5 is H, or alkyl of 1 to 4 carbon atoms;
R^6 is H, alkyl of 1 to 5 carbon atoms; OR^9; or $NR^{10}R^{11}$;
R^7 is H, alkyl of 1 to 4 carbon atoms, or acyl of 1 to 4 carbon atoms;
R^8 is CF_3, alkyl of 1 to 6 carbon atoms or phenyl;
m is 1 to 5.

with the proviso that when X^1 = H then X^2 is not



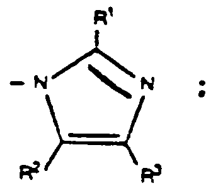
6. The process of Claim 5 wherein X^2 is Br or



wherein
R^1 is alkyl of 3 to 7 carbon atoms;
R^2 is $-(CH_2)_mOR^4$ where m is 1 to 5 and R^4 is H or alkyl of 1 to 4 carbon atoms; and
R^3 is Cl.

7. The process of Claim 6 wherein X^2 is Br.

8. The process of Claim 6 wherein X^2 is

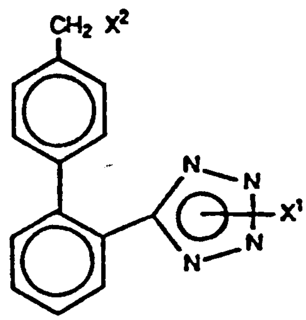


wherein R^1, R^2 and R^3 are as defined in Claim 6.

9. The process of Claim 8 wherein R^1 is n-butyl, R^2 is $-CH_2OH$ and R^3 is Cl.

Patentansprüche
Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE

1. Tetrazol der Formel

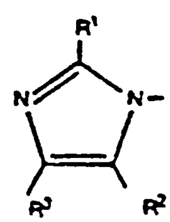


(I) ,

worin

X^1 H, $Sn(R)_3$, -C(Phenyl)$_3$, p-Nitrobenzyl oder ß-Propionitril ist;

X^2 Cl, Br, I, O-Tosyl, OH, O-Mesyl oder



ist;

R Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Phenyl oder Cyclohexyl ist;

R^1 Alkyl mit 3 bis 10 Kohlenstoff-Atomen, Alkenyl mit 3 bis 10 Kohlenstoff-Atomen, Alkinyl mit 3 bis 10 Kohlenstoff-Atomen und Benzyl ist, das mit bis zu 2 Gruppen substituiert ist, die aus Alkoxy mit 1 bis 4 Kohlenstoff-Atomen, Halogen, Alkyl mit 1 bis 4 Kohlenstoff-Atomen, Nitro und Amino ausgewählt sind;

R^2 Phenylalkenyl, worin der aliphatische Teil aus 2 bis 4 Kohlenstoff-Atomen besteht,-$(CH_2)_m$-Imidazoyl-1-yl, -$(CH_2)_m$-1,2,3-Triazolyl, das gegebenenfalls durch eine oder zwei aus CO_2CH_3 und Alkyl mit 1 bis 4 Kohlenstoff-Atomen ausgewählte Gruppen substituiert ist, -$(CH_2)_m$-Tetrazolyl, -$(CH_2)_nOR^4$,

$-(CH_2)_nO\overset{O}{\overset{\|}{C}}R^5$, $-CH{=}CH(CH_2)_s\overset{O}{\overset{\|}{C}}R^6$,

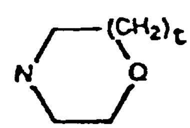
$-CH{=}CH(CH_2)_s\underset{R^5}{\underset{|}{C}}HOR^7$, $-(CH_2)_n\overset{O}{\overset{\|}{C}}R^6$, $-(CH_2)_nNH\overset{O}{\overset{\|}{C}}{-}OR^8$,

$-(CH_2)_nNHSO_2\text{-}OR^8$, $-(CH_2)_mF$,

$-\overset{O}{\overset{\|}{C}}R^6$

ist;

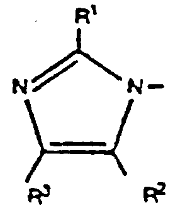
R^3	H, F, Cl, Br, I, NO_2, CF_3 oder CN ist;
R^4	H, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen, Phenyl oder Benzyl ist;
R^5	H, Alkyl oder Perfluoralkyl mit 1 bis 8 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen, Phenyl oder Benzyl ist;
R^6	H, Alkyl mit 1 bis 5 Kohlenstoff-Atomen, OR^9 oder $NR^{10}R^{11}$ ist;
R^7	H, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen, Phenyl, Benzyl, Acyl mit 1 bis 4 Kohlenstoff-Atomen, Phenacyl ist;
R^8	Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Perfluoralkyl mit 1 bis 6 Kohlenstoff-Atomen, 1-Adamantyl, 1-Naphthyl, 1-(1-Naphthyl)ethyl oder $(CH_2)_pC_6H_5$ ist;
R^9	H, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen oder Phenyl ist;
R^{10} und R^{11}	unabhängig H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen, Phenyl, Benzyl sind oder, zusammen genommen, einen Ring der Formel



bilden;

Q	NR^{12}, O oder CH_2 ist;
R^{12}	H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen oder Phenyl ist;
m	1 bis 5 ist,
n	1 bis 10 ist,
s	0 bis 5 ist,
p	0 bis 3 ist,
t	0 bis 1 ist,

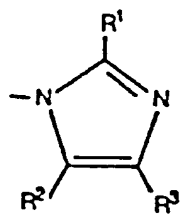
mit der Maßgabe, daß dann, wenn X^1 = H, X^2 nicht



sein kann.

2. Tetrazol nach Anspruch 1, worin X^1 H, $Sn(R)_3$ oder -C(Phenyl)$_3$ ist, worin R Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist.

3. Tetrazol nach Anspruch 1, worin X^2 Br, Cl oder



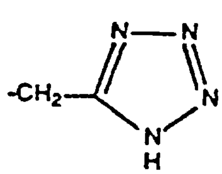
ist; worin R^1, R^2 und R^3 die in Anspruch 1 angegebenen Bedeutungen haben.

4. Tetrazol nach Anspruch 3, worin
   R^1 Alkyl, Alkenyl oder Alkinyl mit 3 bis 7 Kohlenstoff-Atomen ist,
   R^2 -$(CH_2)_mOR^4$,

$$-(CH_2)_mO\overset{\overset{\displaystyle O}{\|}}{C}R^5,\quad -CH{=}CH-\overset{\overset{\displaystyle R^5}{|}}{C}HOR^7,$$

$$-(CH_2)_m\overset{\overset{\displaystyle O}{\|}}{C}-R^6,\quad -CH_2NH\overset{\overset{\displaystyle O}{\|}}{C}OR^8,$$

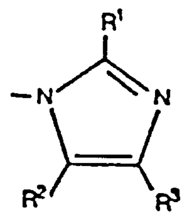
-$(CH_2)_mNHSO_2R^8$,


oder $-\overset{\overset{\displaystyle O}{\|}}{C}R^6$

ist;
   R^3 H, Cl, Br oder I ist;

R^4 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R^5 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R^6 H, Alkyl mit 1 bis 5 Kohlenstoff-Atomen, OR^9 oder $NR^{10}R^{11}$ ist;
R^7 H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen oder Acyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R^8 CF_3, Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist;
m 1 bis 5 ist.

5. Tetrazol nach Anspruch 1, worin
X^1 H, $Sn(R)_3$ oder $-C(Phenyl)_3$ ist, worin R Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist,
X^2 Br, Cl oder

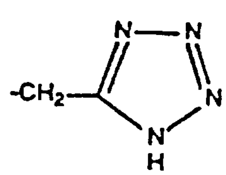


ist;
worin
R^1 Alkyl, Alkenyl oder Alkinyl mit 3 bis 7 Kohlenstoff-Atomen ist,
R^2 $-(CH_2)_mOR^4$,

$$-(CH_2)_mO\overset{O}{\overset{\|}{C}}R^5, \quad -CH{=}CH-\overset{R^5}{\overset{|}{C}}HOR^7,$$

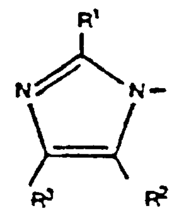
$$-(CH_2)_m\overset{O}{\overset{\|}{C}}-R^6, \quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8,$$

$-(CH_2)_mNHSO_2R^8$,



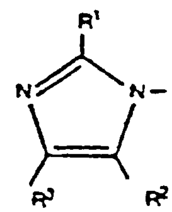
$$\text{oder } -\overset{O}{\overset{\|}{C}}R^6$$

ist;
R^3 H, Cl, Br oder I ist;
R^4 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R^5 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R^6 H, Alkyl mit 1 bis 5 Kohlenstoff-Atomen, OR^9 oder $NR^{10}R^{11}$ ist;
R^7 H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen oder Acyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R^8 CF_3, Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist;
m 1 bis 5 ist,
mit der Maßgabe, daß dann, wenn X^1 = H, X^2 nicht



ist.

6. Tetrazol nach Anspruch 5, worin X^2 Br oder

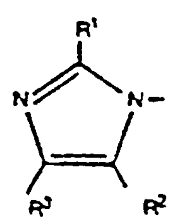


ist, worin

- R^1 Alkyl mit 3 bis 7 Kohlenstoff-Atomen ist,
- R^2 $-(CH_2)_mOR^4$ ist, worin
- m 1 bis 5 ist und
- R^4 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist und
- R^3 Cl ist.

7. Tetrazol nach Anspruch 6, worin X^2 Br ist.

8. Tetrazol nach Anspruch 6, worin X^2



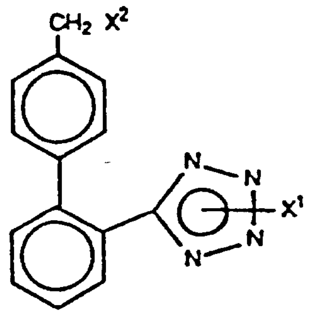
ist, worin R^1, R^2 und R^3 die in Anspruch 6 angegebenen Bedeutungen haben.

9. Tetrazol nach Anspruch 8, worin

- R^1 n-Butyl ist,
- R^2 $-CH_2OH$ ist und
- R^3 Cl ist.

Patentansprüche für folgenden Vertragsstaat : ES

1. Verfahren zur Herstellung eines Tetrazols der Formel

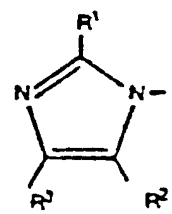


(I) ,

worin

X^1 H, $Sn(R)_3$, -C(Phenyl)$_3$, p-Nitrobenzyl oder ß-Propionitril ist;

X^2 Cl, Br, I, O-Tosyl, OH, O-Mesyl oder



ist;

R Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Phenyl oder Cyclohexyl ist;

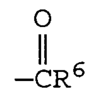
R^1 Alkyl mit 3 bis 10 Kohlenstoff-Atomen, Alkenyl mit 3 bis 10 Kohlenstoff-Atomen, Alkinyl mit 3 bis 10 Kohlenstoff-Atomen und Benzyl ist, das mit bis zu 2 Gruppen substituiert ist, die aus Alkoxy mit 1 bis 4 Kohlenstoff-Atomen, Halogen, Alkyl mit 1 bis 4 Kohlenstoff-Atomen, Nitro und Amino ausgewählt sind;

R^2 Phenylalkenyl, worin der aliphatische Teil aus 2 bis 4 Kohlenstoff-Atomen besteht, -$(CH_2)_m$-Imidazoyl-1-yl, -$(CH_2)_m$-1,2,3-Triazolyl, das gegebenenfalls durch eine oder zwei aus CO_2CH_3 und Alkyl mit 1 bis 4 Kohlenstoff-Atomen ausgewählte Gruppen substituiert ist, -$(CH_2)_m$-Tetrazolyl, -$(CH_2)_nOR^4$,

$$-(CH_2)_nO\overset{\overset{\displaystyle O}{\|}}{C}R^5,\quad -CH{=}CH(CH_2)_s\overset{\overset{\displaystyle O}{\|}}{C}R^6,$$

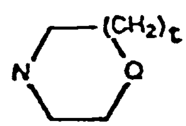
$$-CH{=}CH(CH_2)_s\underset{\underset{\displaystyle R^5}{|}}{C}HOR^7,\quad -(CH_2)_n\overset{\overset{\displaystyle O}{\|}}{C}R^6,\quad -(CH_2)_nNH\overset{\overset{\displaystyle O}{\|}}{C}{-}OR^8,$$

-$(CH_2)_nNHSO_2$-OR^8, -$(CH_2)_mF$,



ist;

R^3	H, F, Cl, Br, I, NO_2, CF_3 oder CN ist;
R^4	H, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen, Phenyl oder Benzyl ist;
R^5	H, Alkyl oder Perfluoralkyl mit 1 bis 8 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen, Phenyl oder Benzyl ist;
R^6	H, Alkyl mit 1 bis 5 Kohlenstoff-Atomen, OR^9 oder $NR^{10}R^{11}$ ist;
R^7	H, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen, Phenyl, Benzyl, Acyl mit 1 bis 4 Kohlenstoff-Atomen, Phenacyl ist;
R^8	Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Perfluoralkyl mit 1 bis 6 Kohlenstoff-Atomen, 1-Adamantyl, 1-Naphthyl, 1-(1-Naphthyl)ethyl oder $(CH_2)_pC_6H_5$ ist;
R^9	H, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Cycloalkyl mit 3 bis 6 Kohlenstoff-Atomen oder Phenyl ist;
R^{10} und R^{11}	unabhängig H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen, Phenyl, Benzyl sind oder, zusammen genommen, einen Ring der Formel



bilden;

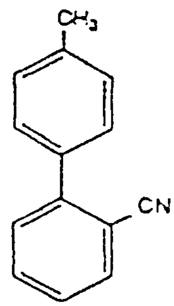
Q	NR^{12}, O oder CH_2 ist;
R^{12}	H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen oder Phenyl ist;
m	1 bis 5 ist,
n	1 bis 10 ist,
s	0 bis 5 ist,
p	0 bis 3 ist,
t	0 bis 1 ist,

wobei

a) Verbindungen der Formel (I), worin

X^1	$Sn(R)_3$ ist und R Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist und
X^2	Imidazoyl ist, worin
R^1	n-Butyl ist,
R^3	Cl ist und
R^2	Hydroxymethyl ist,

durch die 1,3-dipolare Cycloaddition von Trialkylzinn- oder Triphenylzinnaziden an das in geeigneter Weise substituierte Nitril (II)



(II)

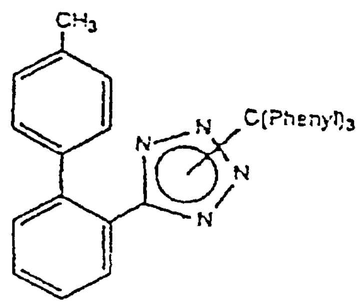
hergestellt werden können;

b) Verbindungen der Formel (I), worin

X^1 C(Phenyl)$_3$ ist und

X^2 Br ist,

durch radikalische Bromierung von (VII)



(VII)

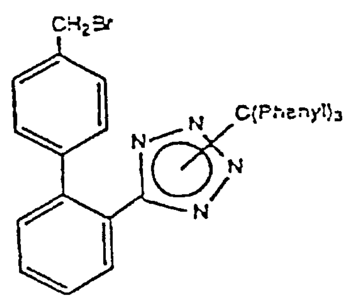
mit N-Bromsuccinimid (NBS) und Dibenzoylperoxid (Bz_2O_2) hergestellt werden können;

c) Verbindungen der Formel (I), worin

X^1 C(Phenyl)$_3$ ist und

X^2 I ist,

durch Austausch des Brom-Bausteins (XII)



(XII)

mit Natriumiodid in Aceton unter Standard-Bedingungen hergestellt werden können;

d) Verbindungen der Formel (I), worin

X^1 C(Phenyl)$_3$ ist und

X^2 OH ist,

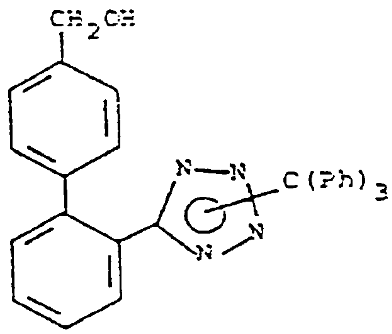
durch eine Austausch-Reaktion des Bromids in der Formel (XII) gegen ein Hydroxid-Ion erhalten werden können;

e) Verbindungen der Formel (I), worin

X^1 C(Phenyl)$_3$ ist und

X^2 das Chlorid ist,

durch Reaktion des Alkohols (XIV)



(XIV)

mit Kohlenstofftetrachlorid und Triphenylphosphin erhalten werden können;

e) Verbindungen der Formel (I), worin

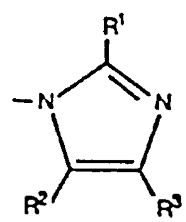
X^1 C(Phenyl)$_3$ ist und

X^2 das Tosylat oder Mesylat ist,

durch Reaktion des Alkohols (XIV) mit p-Toluolsulfonylchlorid bzw. Methansulfonylchlorid in Pyridin unter Standard-Bedingungen erhalten werden können.

2. Verfahren nach Anspruch 1, worin X^1 H, Sn(R)$_3$ oder -C(Phenyl)$_3$ ist, worin R Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist.

3. Verfahren nach Anspruch 1, worin X^2 Br, Cl oder



ist; worin R^1, R^2 und R^3 die in Anspruch 1 angegebenen Bedeutungen haben.

4. Verfahren nach Anspruch 3, worin

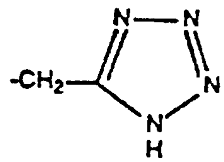
R^1 Alkyl, Alkenyl oder Alkinyl mit 3 bis 7 Kohlenstoff-Atomen ist,

R^2 $-(CH_2)_mOR^4$,

$$-(CH_2)_m O\overset{\overset{O}{\|}}{C}R^5, \quad -CH{=}CH-\overset{\overset{R^5}{|}}{C}HOR^7,$$

$$-(CH_2)_m\overset{\overset{O}{\|}}{C}-R^6, \quad -CH_2NH\overset{\overset{O}{\|}}{C}OR^8,$$

$-(CH_2)_mNHSO_2R^8$,

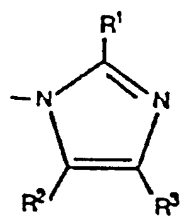
 oder $-\overset{\displaystyle O}{\overset{\|}{C}}R^6$

ist;

- R^3 H, Cl, Br oder I ist;
- R^4 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
- R^5 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
- R^6 H, Alkyl mit 1 bis 5 Kohlenstoff-Atomen, OR^9 oder $NR^{10}R^{11}$ ist;
- R^7 H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen oder Acyl mit 1 bis 4 Kohlenstoff-Atomen ist;
- R^8 CF_3, Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist;
- m 1 bis 5 ist.

5. Verfahren nach Anspruch 1, worin

- X^1 H, $Sn(R)_3$ oder $-C(Phenyl)_3$ ist, worin R Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist,
- X^2 Br, Cl oder



ist;

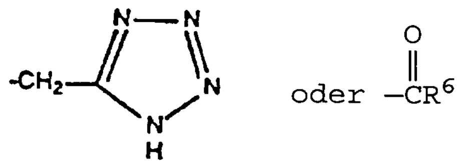
worin

- R^1 Alkyl, Alkenyl oder Alkinyl mit 3 bis 7 Kohlenstoff-Atomen ist,
- R^2 $-(CH_2)_mOR^4$,

$$-(CH_2)_mO\overset{\displaystyle O}{\overset{\|}{C}}R^5,\quad -CH{=}CH-\overset{\displaystyle R^5}{\overset{|}{C}}HOR^7,$$

$$-(CH_2)_m\overset{\displaystyle O}{\overset{\|}{C}}-R^6,\quad -CH_2NH\overset{\displaystyle O}{\overset{\|}{C}}OR^8,$$

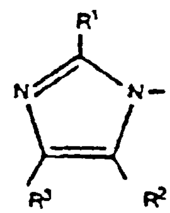
$-(CH_2)_mNHSO_2R^8$,



ist;

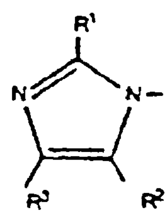
R³ H, Cl, Br oder I ist;
R⁴ H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R⁵ H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R⁶ H, Alkyl mit 1 bis 5 Kohlenstoff-Atomen, OR^9 oder $NR^{10}R^{11}$ ist;
R⁷ H, Alkyl mit 1 bis 4 Kohlenstoff-Atomen oder Acyl mit 1 bis 4 Kohlenstoff-Atomen ist;
R⁸ CF_3, Alkyl mit 1 bis 6 Kohlenstoff-Atomen oder Phenyl ist;
m 1 bis 5 ist,

mit der Maßgabe, daß dann, wenn X^1 = H, X^2 nicht



ist.

6. Verfahren nach Anspruch 5, worin X^2 Br oder

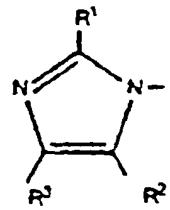


ist, worin

R^1 Alkyl mit 3 bis 7 Kohlenstoff-Atomen ist,
R^2 $-(CH_2)_mOR^4$ ist, worin
m 1 bis 5 ist und
R^4 H oder Alkyl mit 1 bis 4 Kohlenstoff-Atomen ist und
R^3 Cl ist.

7. Verfahren nach Anspruch 6, worin X^2 Br ist.

8. Verfahren nach Anspruch 6, worin X^2



ist, worin R^1, R^2 und R^3 die in Anspruch 6 angegebenen Bedeutungen haben.

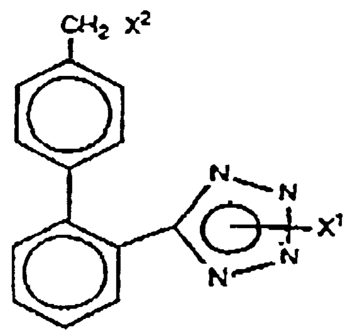
9. Verfahren nach Anspruch 8, worin

R^1 n-Butyl ist,
R^2 $-CH_2OH$ ist und
R^3 Cl ist.

Revendications

Revendications pour les Etats contractants suivants : AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE

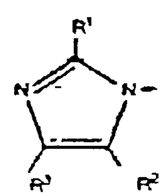
1. Un tétrazole présentant la formule:



(I)

dans laquelle :

X^1 est H, $Sn(R)_3$, $-C(\text{phényl})_3$, p-nitrobenzyl ou β-propionitrile,
X^2 est Cl, Br, I, o-tosyl, OH, o-mesyl, ou



;

R est un radical alkyl comprenant 1 à 6 atomes de carbone, phényl ou cyclohexyl;
R^1 est radical alkyl comprenant 3 à 10 atomes de carbone, alkynyl comprenant 3 à 10 atomes de carbone, et benzyl substitué jusqu'à deux groupes choisis parmi les radicaux alkoxy comprenant 1 à 4 atomes de carbone, alkyl comprenant 1 à 4 atomes de carbone atomes d'halogène ou les résidus nitro et amino;
R^2 est un radical phénylalkényl dont la partie aliphatique comprend 2 à 4 atomes de carbone, $-(CH_2)_m$-imidazoyl-1-yl, $-(CH_2)_m$-1,2,3-triazolyl éventuellement substitué par un ou deux groupes choisis parmi CO_2CH_3 et les radicaux alkyl comprenant 1 à 4 atomes de carbone, $(CH_2)_m$-tétraolyl, $-(CH_2)_nOR^4$;

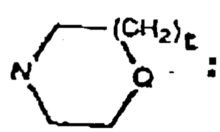
$$-(CH_2)_nO\overset{O}{\overset{\|}{C}}R^5;\quad -CH{=}CH(CH_2)_s\overset{O}{\overset{\|}{C}}R^6;$$

$$-CH{=}CH(CH_2)_s\underset{R_5}{CH}OR^7;\quad -(CH_2)_n\overset{O}{\overset{\|}{C}}R^6;\quad -(CH_2)_nNH\overset{O}{\overset{\|}{C}}{-}OR^8;$$

$-(CH_2)_nNHSO_2R_8$ $-(CH_2)_mF$;

$$-\overset{O}{\overset{\|}{C}}R^6$$

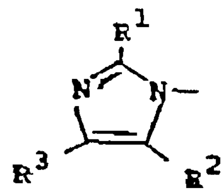
R^3	est H, F, Cl, Br, I, NO_2; CF_3, ou CN;
R^4	est H, radical alkyl comprenant 1 à 6 atomes de carbone, cycloakyl comprenant 3 à 6 atomes de carbone, phényl ou benzyl;
R^5	est H, radical alkyl ou perfluoroalkyl comprenant 1 à 8 atomes de carbone, cycloakyl comprenant 3 à 6 atomes de carbone, phényl ou benzyl;
R^6	est H, radical alkyl comprenant 1 à 5 atomes de carbone, OR^9 ou $NR^{10}R^{11}$;
R^7	est H, radical alkyl comprenant 1 à 6 atomes de carbone, cycloalkyl comprenant 3 à 6 atomes de carbone, phényl, benzyl, acyl comprenant 1 à 4 atomes de carbone, ou phénacyl;
R^8	est un radical alkyl de 1 à 6 atomes de carbone ou un perfluoroalkyl de 1 à 6 atomes de carbone, 1-adamantyl, 1-naphthyl, 1-(1-naphthyl)éthyl, ou $(CH_2)_pC_6H_5$;
R^9	est H, un radical alkyl comprenant 1 à 6 atomes de carbone, cycloalkyl comprenant 3 à 6 atomes de carbone, ou un phényl;
R^{10} et R^{11}	indépendamment l'un de l'autre, consistent en H, un radical alkyl comprenant 1 à 4 atomes de carbone, phényl, banzyl ou, pris ensemble, forment un cycle de formule



dans laquelle :

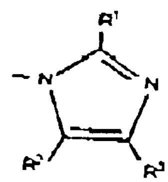
Q	est NR^{12}, O, ou CH_2;
R^{12}	est H, un radical alkyl comprenant 1 à 4 atomes de carbone, ou un phényl;
m	est de 1 à 5;
n	est de 1 à 10;
s	est de 0 à 5;
p	est de 0 à 3;
t	est 0 ou 1,

à la condition que lorsque X^1 est un atome hydrogène, X^2 ne soit pas le groupe



2. Le tétrazole selon la revendication 1, dans lequel X^1 est un atome hydrogène, $Sn(R)_3$ ou -C(phényl)$_3$, R étant un radical alkyl comprenant 1 à 6 atomes de carbone ou un radical phényl.

3. Le tétrazole selon la revendication 1, dans lequel X^2 est Br, Cl ou



R^1, R^2, R^3 étant tels que définis dans la revendication 1.

4. Le tétrazole selon la revendication 3, dans lequel

R^1	est un radical alkyl, alkenyl ou alkynyl comprenant 3 à 7 atomes de carbone;
R^2	est $-(CH_2)_mOR^4$;

$$-(CH_2)mO\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH-\overset{R^5}{\overset{|}{C}}HOR^7$$

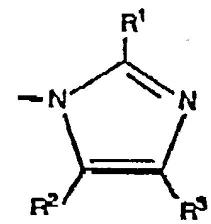
$$-(CH_2)_m\overset{O}{\overset{\|}{C}}-R^6; \quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8;$$

$-(CH_2)_mNHSO_2R^8$; $-(CH_2)_mF$; ou

$$-\overset{O}{\overset{\|}{C}}R_6 \ ;$$

R^3	est H, Cl, Br, ou I;
R^4	est H, ou un radical alkyl contenant 1 à 4 atomes de carbone;
R^5	est H, ou un radical alkyl contenant 1 à 4 atomes de carbone;
R^6	est H, ou un radical alkyl contenant 1 à 5 atomes de carbone; OR^9; ou $NR^{10}R^{11}$;
R7	est H, ou un radical alkyl contenant 1 à 4 atomes de carbone, ou un radical acyl contenant 1 à 4 atomes de carbone;
R8	est CF_3, un radical alkyl contenant 1 à 6 atomes de carbone ou un phényl;
m	a une valeur de 1 à 5.

5. Le tétrazole selon la revendication 1, dans lequel X^1 est H,$Sn(R_3)$ ou -C(phényl)$_3$ où R est un radical alkyl comprenant 1 à 6 atomes de carbone ou un radical phényl, et X^2 est Br, Cl ou



où

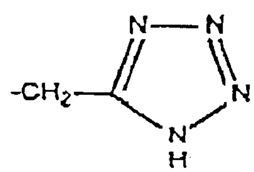
R¹ est un alkyl, un alkenyl ou un alkynyl comprenant 3 à 7 atomes de carbone;

R² est $-(CH_2)_mOR^4$;

$-(CH_2)_mO\overset{O}{\overset{\|}{C}}R^5$; $-CH{=}CH-\overset{R^5}{\overset{|}{C}}HOR^7$

$-(CH2)_m\overset{O}{\overset{\|}{C}}-R^6$; $-CH_2NH\overset{O}{\overset{\|}{C}}OR^8$;

$-(CH_2)_mNHSO_2R^8$;

 ; or $-\overset{O}{\overset{\|}{C}}R^6$;

R^3 est H, Cl, Br, ou I;

R^4 est H, ou un radical comprenant de 1 à 4 atomes de carbone;

R^5 est H, ou un radical alkyl comprenant de 1 à 4 atomes de carbone;

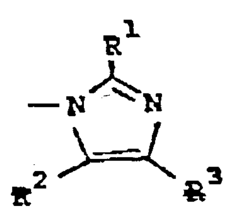
R^6 est H, un radical alkyl comprenant de 1 à 5 atomes de carbone, OR^9; ou $NR^{10}R^{11}$;

R^7 est H, ou un radical alkyl comprenant de 1 à 4 atomes de carbone, ou un radical acyl comprenant de 1 à 4 atomes de carbone;

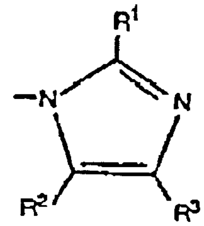
R^8 est CF_3, un radical alkyl comprenant de 1 à 6 atomes de carbone ou un phényl;

m a une valeur de 1 à 5;

étant entendu que lorsque $X^1 = H$, X^2 ne soit pas le groupe



6. Le tétrazole selon la revendication 5, dans lequel X^2 est Br ou

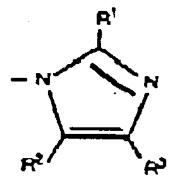


dans laquelle

- R^1 est un radical alkyl comprenant de 3 à 7 atomes de carbone;
- R^2 est $-(CH_2)_mOR^4$ avec m ayant pour valeur 1 à 5 et R^4 étant H, ou un radical du groupe alkyl comprenant 1 à 4 atomes de carbone; et
- R^3 est Cl.

7. Le tétrazole selon la revendication 6, dans lequel X^2 est Br.

8. Le tétrazole selon la revendication 6, dans lequel X^2 est

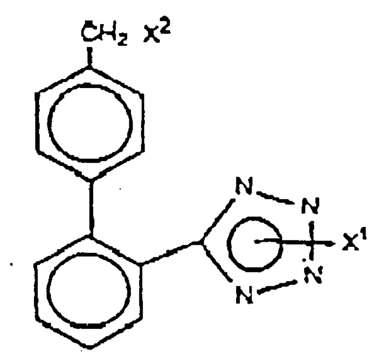
 ;

où R^1, R^2, et R^3 sont tels que définis dans la revendication 6.

9. Le tétrazole selon la revendication 8, dans lequel R^1 est n-butyl, R^2 est $-CH_2OH$ et R^3 est Cl.

Revendications pour l'Etat contractant suivant : ES

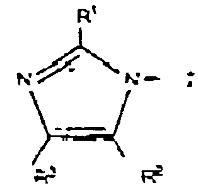
1. Un procédé pour la fabrication de tétrazole présentant la formule:



(I)

dans laquelle :

- X^1 est H, $Sn(R)_3$, $-C(\text{phényl})_3$, p-nitrobenzyl ou β-propionitrile,
- X^2 est Cl, Br, I, o-tosyl, OH, o-mesyl, ou



R est un radical alkyl comprenant 1 à 6 atomes de carbone, phényl ou cyclohexyl;

R^1 est radical alkyl comprenant 3 à 10 atomes de carbone, alkynyl comprenant 3 à 10 atomes de carbone, et benzyl substitué jusqu'à deux groupes choisis parmi les radicaux alkoxy comprenant 1 à 4 atomes de carbone, alkyl comprenant 1 à 4 atomes de carbone, atomes d'halogène ou les résidus nitro et amino;

R^2 est un radical phénylalkényl dont la partie aliphatique comprend 2 à 4 atomes de carbone, $-(CH_2)_m$-imidazoyl-1-yl, $-(CH_2)_m$-1,2,3-triazolyl éventuellement substitué par un ou deux groupes choisis parmi CO_2CH_3 et les radicaux alkyl comprenant 1 à 4 atomes de carbone, $(CH_2)_m$-tétrazolyl,$-(CH_2)_nOR^4$;

$$-(CH_2)_n O\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH(CH_2)_s\overset{O}{\overset{\|}{C}}R^6;$$

$$-CH{=}CH(CH_2)_s\underset{R_5}{\underset{|}{C}}HOR^7; \quad -(CH_2)_n\overset{O}{\overset{\|}{C}}R^6; \quad -(CH_2)_nNH\overset{O}{\overset{\|}{C}}-OR^8;$$

$-(CH_2)_nNHSO_2R_8$ $-(CH_2)_mF$;

$$-\overset{O}{\overset{\|}{C}}R^6$$

R^3 est H, F, Cl, Br, I, NO_2; CF_3, ou CN;

R^4 est H, radical alkyl comprenant 1 à 6 atomes de carbone, cycloakyl comprenant 3 à 6 atomes de carbone, phényl ou benzyl;

R^5 est H, radical alkyl ou perfluoroalkyl comprenant 1 à 8 atomes de carbone, cycloakyl comprenant 3 à 6 atomes de carbone, phényl ou benzyl;

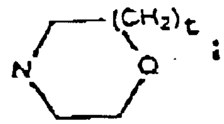
R^6 est H, radical alkyl comprenant 1 à 5 atomes de carbone, OR^9 ou $NR^{10}R^{11}$;

R^7 est H, radical alkyl comprenant 1 à 6 atomes de carbone, cycloalkyl comprenant 3 à 6 atomes de carbone, phényl, benzyl, acyl comprenant 1 à 4 atomes de carbone, ou phénacyl;

R^8 est un radical alkyl de 1 à 6 atomes de carbone ou un perfluoroalkyl de 1 à 6 atomes de carbone, 1-adamantyl, 1-naphthyl, 1-(1-naphthyl)éthyl, ou $(CH_2)_pC_6H_5$;

R^9 est H, un radical alkyl comprenant 1 à 6 atomes de carbone, cycloalkyl comprenant 3 à 6 atomes de carbone, ou un phényl;

R^{10} et R^{11} indépendamment l'un de l'autre, consistent en H, un radical alkyl comprenant 1 à 4 atomes de carbone, phényl, banzyl ou, pris ensemble, forment un cycle de formule

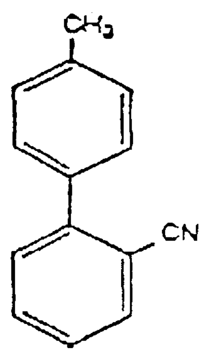


dans laquelle :

Q	est NR^{12}, O, ou CH_2;
R^{12}	est H, un radical alkyl comprenant 1 à 4 atomes de carbone, ou un phényl;
m	est de 1 à 5;
n	est de 1 à 10;
s	est de 0 à 5;
p	est de 0 à 3;
t	est 0 ou 1,

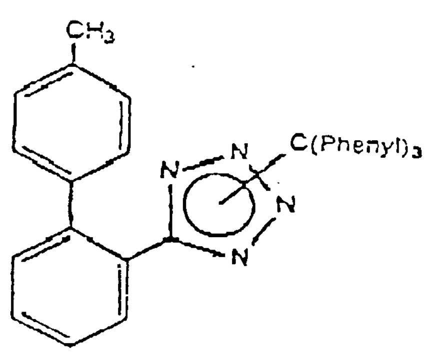
dans lequel

a) les composés de la formule (I), dans laquelle X^1 est $Sn(R)_3$ et R est un radical alkyl comprenant de 1 à 6 atomes de carbone ou un radical phényl et X^2 est un le radical imidazoyl dans lequel R^1 est radical n-butyl, R^3 est un atome de chlore, et R^2 un radical hydroxyméthyl peuvent être préparés par la cycloaddition 1,3-dipolaire d'azidures de trialkylétain ou d'azidures de triphénylétain au nitrile substitué convenable (II)



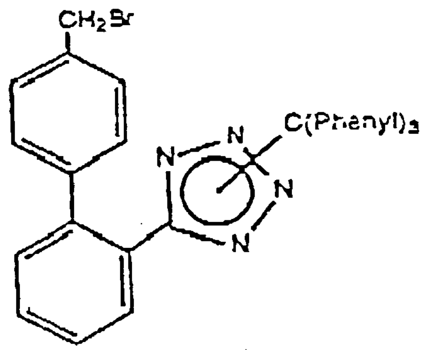
(II)

b) les composés de la formule (I) dans laquelle X^1 est un radical C(phényl)$_3$ et X^2 est un atome de brome peuvent être préparés par bromation radicalaire de (VII) N-bromosuccinimide (NBS) et dibenzoylperoxyde (Bz_2O_2)



(VII)

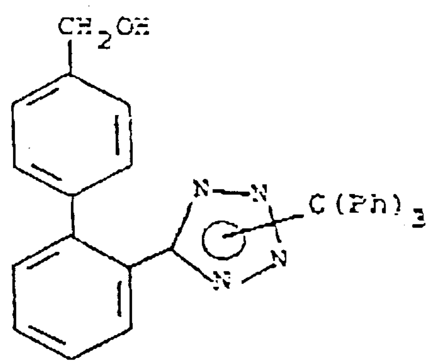
c) les composés de la formule (I) dans laquelle X^1 est un radical C(phényl)$_3$ et X^2 est I peuvent être préparés par déplacement de l'atome de brome en (XII) à l'aide de iodure de sodium dans l'acétone dans les conditions standard;



(XII)

d) les composés de la formule (I) dans laquelle X^1 est un radical C(phényl)$_3$ et X^2 est un groupe OH peuvent être obtenus par réaction du déplacement du brome dans la formule (XII) à l'aide d'un ion hydroxyde;

e) les composés de la formule (I) dans laquelle X^1 est un radical C(phényl)$_3$ et X^2 est atome de chlore peuvent être obtenu par réaction de l'alcool (XIV)



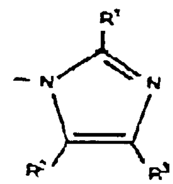
(XIV)

avec du tétrachlorure de carbone et du triphénylphosphine;

f) les composés de la formule (I) dans laquelle X^1 est un radical C(phényl)$_3$ et X^2 est du tosylate ou du mésylate peuvent être obtenus par réaction de l'alcool (XIV) avec du chlorure de p-toluènesulfonyl ou du chlorure de méthanesulfonyl, respectivement dans de la pyridine dans des conditions standard.

2. Le procédé pour la fabrication de tétrazole selon la revendication 1, dans lequel X^1 est un atome hydrogène, Sn(R)$_3$ ou -C(phényl)$_3$, R étant un radical alkyl comprenant 1 à 6 atomes de carbone ou un radical phényl.

3. Le procédé pour la fabrication de tétrazole selon la revendication 1, dans lequel X^2 est Br, Cl ou



R^1, R^2, R^3 étant tels que définis dans la revendication 1.

4. Le procédé pour la fabrication de tétrazole selon la revendication 3, dans lequel

- R^1 est un radical alkyl, alkenyl ou alkynyl comprenant 3 à 7 atomes de carbone;
- R^2 est $-(CH_2)_mOR^4$;

$$-(CH_2)_mO\overset{O}{\overset{\|}{C}}R^5; \quad -CH{=}CH-\overset{R^5}{\overset{|}{C}}HOR^7$$

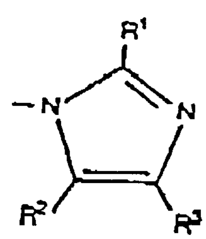
$$-(CH_2)_m\overset{O}{\overset{\|}{C}}-R^6; \quad -CH_2NH\overset{O}{\overset{\|}{C}}OR^8;$$

$-(CH_2)_mNHSO_2R^8$; $-(CH_2)_mF$; ou

$$-\overset{O}{\overset{\|}{C}}R_6 \;;$$

- R^3 est H, Cl, Br, ou I;
- R^4 est H, ou un radical alkyl contenant 1 à 4 atomes de carbone;
- R^5 est H, ou un radical alkyl contenant 1 à 4 atomes de carbone;
- R^6 est H, ou un radical alkyl contenant 1 à 5 atomes de carbone; OR^9; ou $NR^{10}R^{11}$;
- R7 est H, ou un radical alkyl contenant 1 à 4 atomes de carbone, ou un radical acyl contenant 1 à 4 atomes de carbone;
- R8 est CF_3, un radical alkyl contenant 1 à 6 atomes de carbone ou un phényl;
- m a une valeur de 1 à 5.

5. Le procédé pour la fabrication de tétrazole selon la revendication 1, dans lequel X^1 est H,$Sn(R_3)$ ou -C-(phényl)$_3$ où R est un radical alkyl comprenant 1 à 6 atomes de carbone ou un radical phényl, et X^2 est Br, Cl ou



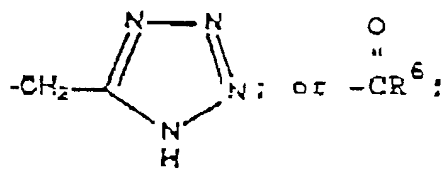
où

- R^1 est un alkyl, un alkenyl ou un alkynyl comprenant 3 à 7 atomes de carbone;
- R^2 est $-(CH_2)_mOR^4$;

$-(CH_2)_m O\overset{O}{\overset{\|}{C}}R^5$; $-CH=CH-\overset{R^5}{\overset{|}{C}}HOR^7$

$-(CH2)_m\overset{O}{\overset{\|}{C}}-R^6$; $-CH_2NH\overset{O}{\overset{\|}{C}}OR^8$;

$-(CH_2)_mNHSO_2R^8$;



R³ est H, Cl, Br, ou I;

R^4 est H, ou un radical comprenant de 1 à 4 atomes de carbone;

R^5 est H, ou un radical alkyl comprenant de 1 à 4 atomes de carbone;

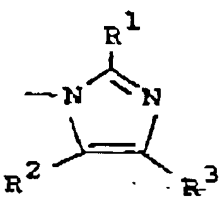
R^6 est H, un radical alkyl comprenant de 1 à 5 atomes de carbone, OR^9; ou $NR^{10}R^{11}$,

R^7 est H, ou un radical alkyl comprenant de 1 à 4 atomes de carbone, ou un radical acyl comprenant de 1 à 4 atomes de carbone;

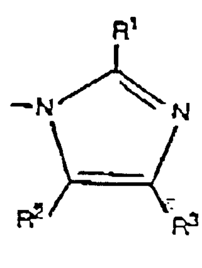
R^8 est CF_3, un radical alkyl comprenant de 1 à 6 atomes de carbone ou un phényl;

m a une valeur de 1 à 5;

étant entendu que lorsque $x^1 = H$, X^2 ne soit pas le groupe



6. Le procédé pour la fabrication de tétrazole selon la revendication 5, dans lequel X^2 est Br ou



dans laquelle

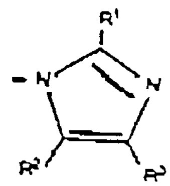
R^1 est un radical alkyl comprenant de 3 à 7 atomes de carbone;

R^2 est $-(CH_2)_mOR^4$ avec m ayant pour valeur 1 à 5 et R^4 étant H, ou un radical du groupe alkyl comprenant 1 à 4 atomes de carbone; et

R^3 est Cl.

7. Le procédé pour la fabrication de tétrazole selon la revendication 6, dans lequel X^2 est Br.

8. Le procédé pour la fabrication de tétrazole selon la revendication 6, dans lequel X^2 est



;

où R^1, R^2 et R^3 sont tels que définis dans la revendication 6.

9. Le procédé pour la fabrication de tétrazole selon la revendication 8, dans lequel R^1 est n-butyl, R^2 est $-CH_2OH$ et R^3 est Cl.